# Labour induction and the need for neonatal monitoring following birth in Iceland 2009-2018

30 ECTS

Margrét Þóra Einarsdóttir

**Ritgerð til meistaragráðu**
**Háskóli Íslands**
**Læknadeild**
**Miðstöð í lýðheilsuvísindum**
**Heilbrigðisvísindasvið**

HÁSKÓLI ÍSLANDS

# Framköllun fæðinga og þörf á eftirliti nýbura eftir fæðingu á Íslandi 2009-2018

Margrét Þóra Einarsdóttir

Ritgerð til meistaragráðu í lýðheilsuvísindum

Umsjónarkennari: Kristjana Einarsdóttir, Ph.D.

Meistaranámsnefnd: Emma Marie Swift, Ph.D.

Læknadeild

Miðstöð í lýðheilsuvísindum

Heilbrigðisvísindasvið Háskóla Íslands

Júní 2021

# Labour induction and the need for neonatal monitoring following birth in Iceland 2009-2018

***30 ECTS***

Margrét Þóra Einarsdóttir

Thesis for the degree of Master of Science

Supervisor: Kristjana Einarsdóttir, Ph.D.

Masters committee: Emma Marie Swift, Ph.D.

Faculty of Medicine

Centre of Public Health Sciences

School of Health Sciences

June 2021

Prentun: Háskólaprent

Reykjavík, Ísland 2021

# Ágrip

**Bakgrunnur**: Tíðni framköllunar fæðinga hefur aukist til muna síðustu áratugi, sérstaklega meðal iðnríkja. Þessi þróun hefur líka átt sér stað á Íslandi, en rannsóknir hafa sýnt að hæsta tíðni framkallaðra fæðinga meðal norðurlandanna sé á Íslandi. Takmarkaðar rannsóknir eru til um áhrifum tímalengdar framköllnunar á fæðingar nýbura. Tíðni framköllunar fæðinga án læknisfræðilegra ábendinga hefur einnig aukist, en rannsóknir hafa bent til ólíkra niðurstaðna um hvort að framköllun fæðinga án lækisfræðilegrar ábendinga hafi áhrif á heilsu nýbura. Í ljósi þess að tíðni framkallaðra fæðinga er há á Íslandi er mikilvægt að hafa afla eins miklum upplýsingum og hægt er um þau áhrif sem framköllun fæðinga getur haft á nýbura.

**Markmið**: Markmið rannsóknarinnar er að skoða hlutfall nýbura sem þurfa á eftirliti að halda eftir fæðingu út frá upphafi fæðingar ásamt lengd framköllunar fæðingar. Einnig verða ábendingar fyrir framköllun skoðaðar með tilliti til eftirlits eftir fæðingu.

**Aðferð**: Gögn voru sótt í Fæðingaskrá Embætti Landlæknis sem heldur utan um upplýsingar um alla nýbura sem fæðast á landinu. Í úrtaki þessara rannsóknar voru allir lifandi fæddir fullburða einburar sem fæddust á Íslandi á árunum 2009-2018. Tíðni nýburaeftirlits var skoðuð eftir upphafi fæðingar, lengd framköllunar fæðingar og ábendingum framköllunar og kí-kvaðrat próf notuð til að bera saman hópana, lagskipt eftir því hvort móðir var frumbyrja eða fjölbyrja. Ábendingar voru greindar út frá ICD-10 kóðum, meðgöngulengd og aldri móður.

**Niðurstöður**: Heildarþýði rannsóknarinnar var 38.443 nýburar. Þar af fæddust 7,593 (19,8%) eftir framkallaða fæðingu. Tölfræðilega marktækur munur var á milli þess hversu mikið eftirlit nýburar þurftu eftir því hvernig upphaf fæðingar var. Lægst eftirlitstíðni á vökudeild var meðal nýburra sem fæddust eftir sjálfkrafa sótt (4,6%) en hæsta eftirlitstíðni á vökudeild var meðal nýbura fædda eftir fæðingu sem var framkölluð (7,3%). Hærri tíðni framkallaðra fæðinga var meðal frumbyrja (21,5%) en fjölbyrja (18,6%) og var eftirlitstíðnin á vökudeild einnig hærri meðal nýbura frumbyrja (9,9%) en nýbura fjölbyrja (5,4%). Marktækur munur fannst einnig eftir því hversu löng framköllun fæðingar var. Hæst eftirlitstíðni á vökudeild var meðal nýbura fædda eftir framköllun sem varði 12-48 klst. (8,6%), borið saman við framkallanir sem stóðu yfir í 12 klst. eða skemur (5,7%) og 48 klst. eða lengur (8,0%). Algengasta ábending fyrir framköllun fæðinga á tímabilinu var meðgöngulengd >41 vika (22,5%), en sú næstalgengasta voru framkallanir fæðinga án læknisfræðilegra ábendinga (19,6%). Nýburar fæddir eftir framköllun fæðinga vegna sykursýki voru með áberandi hæstu líkurnar á því að þurfa á eftirliti á vökudeild að halda (22%).

**Ályktanir**: Nýburar sem fæðast í kjölfar framkallaðrar fæðingar höfðu hærri eftirlitstíðni á vökudeild miðað við sjálfkrafa sótt og valkeisaraskurði. Þetta var sérstaklega greinilegt meðal frumbyrja. Flestar framkallanir fæðinga stóðu yfir í 12-48 klst, en lægsta eftirlitstíðnin á vökudeild var meðal þeirra sem fæddust eftir framköllun sem stóð yfir í minna en 12 klst. Framkallanir án læknisfræðilegrar ábendinga voru næst algengasti flokkur framkallana en þetta kallar á frekari rannsóknir í ljósi þess að gangsetningar hafa verið að aukast á undanförnum áratugum.

## Abstract

**Background**: The labour induction rate has been on the rise during the last decades, especially in industrialised countries. This trend is also occurring in Iceland, and the highest induction rate among the Nordic countries has been measured to be in Iceland. Limited research can be found on the effect of labour induction duration on infants. Elective labour induction is being performed more frequently but studies have found conflicting results on how this affects infants' risk for needing monitoring after birth. Based on the high labour induction rate, it is important to gain as much information as possible about the effects of labour induction on infants born in Iceland.

**Objectives**: To study the rate of the need for infant monitoring based on labour onset and based on labour induction duration. Indications for labour induction will also be examined with regards to infant monitoring.

**Methods**: Data was obtained from the Icelandic Medical Birth Registry, containing information on all births in Iceland. Included in the analysis were live-born, term singletons born in Iceland 2009-2018. Frequencies and likelihoods were calculated, and chi-square tests used to compare labour onset groups and labour induction duration groups, this was also stratified by parity. Indications for indication were identified using ICD-10 codes, gestational age and maternal age.

**Results**: The study population consisted of 38.443 infants. Among those, 7.593 (19,8%) were born after labour induction. There was a statistically significant difference in monitoring rates by labour onset type. The lowest NICU monitoring rate (4,6%) was amongst infants born after spontaneous labour, but the highest rate was among infants born after labour induction (7,3%). Primipara mothers had a higher labour induction rate (21,5%) than multipara mothers (18,6%). Infants born to primipara mothers did also have a higher NICU monitoring rate than infants born to multipara mothers (9,9% vs. 5,4%). Monitoring rates were also significantly different between groups of labour induction duration. The highest NICU monitoring rate was among infants born after a short labour induction duration (8,6%), compared to infants born after a normal labour induction duration (5,7%) and long labour induction duration (8,0%). The most common indication for labour induction was gestational age >41 weeks (22,5%), followed by elective labour induction (19,6%). Infants born after a labour induction performed because the mother had pre-gestational diabetes had noticeably the highest NICU monitoring rate (22%).

**Conclusion**: Infants born after labour induction have a higher rate of NICU monitoring than the other two labour onset groups, and the NICU monitoring rate was especially high among primipara mothers. Most labour induction had a normal duration, but infants born after a short labour induction had the least need for monitoring after birth. Elective induction was the second most common reason for labour induction in Iceland and further research should focus on this area as labour induction is becoming more prevalent.

# Acknowledgements

I would like to thank my supervisor, Kristjana Einarsdóttir, for allof her guidance, knowledge and encouragement throughout the process of writing this thesis. I also thank Emma Marie Swift for all of her support, rapid responses and knowledge in the field. It has been a pleasure getting to work with both of you.

I thank the Directorate of Health for giving me access to the valuable data as well as The Statistical Counselling Centre at the School of Health Sciences for their help.

My brother, Hafsteinn Birgir, has been my greatest cheerleader during this process and has given me endless support and guidance, thank you for all your help. Thanks to my parents and my better half, Hjalti, for the support and motivation. Lastly, I would like to thank my daughter, Sigrún Metta, as she is the one who sparked my interest in this topic, when I had my labour induced giving birth to her.

# Table of Contents

# List of Figures



# List of Tables



# List of Abbreviations

| | |
|---|---|
| AAP | The American Academy of Paediatrics |
| ACOG | The American Congress of Obstetricians and Gynaecologist |
| BMI | Body Mass Index |
| ICD-10 | The International Classification of Diseases, 10th revision |
| ICD-9 | The International Classification of Diseases, 9th revision |
| NCSP | The Nordic Medico-Statistical Committee, the Classification of Surgical Procedures |
| NICU | Neonatal Intensive Care Unit |
| PROM | Prelabour rupture of membranes |
| WHO | World Health Organization |

# 1 Introduction

Induction of labour is the process of artificially stimulating the uterus to start labour (1) and is one of the most frequently performed obstetric procedures in the world (2). There has been an increase in the number of induced labours worldwide over the past several decades, especially in industrialised countries, where approximately one out of four pregnant women undergo labour induction (2, 3). The induction rate in the United States was at an all-time high in 2018 since the start of data recording on labour induction in birth certificates (4).

This increase in labour induction is also occurring in Iceland. The rate of labour induction has increased from 16% in 2007 to 30.5% in 2018 in Iceland. The rate had then been steady from the year 2015 (5). A study from 2015 found that the highest rate for labour induction among the Nordic countries was in Iceland (6).

The reason for this rapid increase is not fully understood and is likely to be multifactorial. An increase in known risk factors, such as obesity, gestational diabetes and advancing maternal age are believed to be contributors. Changes in protocols for hypertension diseases can also contribute to this increase in the rate of labour induction (5). Studies have also shown that various socioeconomic factors that are linked to the expecting mother affect the risk for labour induction. Less advantaged women, in terms of socioeconomic status, are more likely to have their labour induced. Parity is also a known risk factor, where primipara mothers are more likely to have their labour induced compared to multiparas (7).

According to the World Health Organization (WHO), labour induction should usually only be recommended when waiting for spontaneous labour involves more risk for either mother or baby (3). Furthermore, labour induction should only be performed when there is a clear medical indication for it, as it is not thought to be a risk-free procedure (3). In spite of the recommendations of only performing labour induction when there is a clear medical indication for it, studies have found an increase in labour induction for nonmedical reasons, also called elective labour inductions (3, 8, 9). Elective labour inductions have previously been associated with increased caesarean section rates (10). More recent studies have focused on comparing labour induction to expectant management instead of comparing labour induction to spontaneous labour. These studies do not find this association (11-13), and some guidelines and practices have changed their recommendations for labour induction following the publication of these results.

Labour induction seems to prolong the mean duration time in the latent labour phase (14). Labour induction duration has been linked to the reason for induction, with a higher proportions of deliveries within 24 hours among women having an labour induction based on medical reasons compared to non-medical reasons (15).

In light of the high induction rate in Iceland, it is important to gain as much knowledge as possible on this matter in Icelandic settings. This study will view how the type of labour onset affects infants need for monitoring after birth in Iceland. In addition to examining labour onset rates, labour induction duration and the reasons behind the induction will be viewed with regards to infants need for monitoring after birth.

## 1.1 Labour induction methods

### 1.1.1 Labour induction over the century

The British textbook "Obstetrics" by Ten Teachers was first published in 1917 and is now on its 20th edition (16). The textbook provides a good overview of the evolution of labour induction throughout the century. Labour induction methods early in the century were dangerous both for mothers and infants and were only conducted in the event of life-threatening maternal diseases. Vaginal caesarean section and forced dilatation of the cervix, using either fingers or a metal screw-dilator are mentioned among the labour induction methods used when the first textbooks were published. As the induction methods evolved and safer caesarean sections became available, the threshold for labour induction has been reduced, resulting in labour induction being one of the most common intervention in pregnancy (17).

### 1.1.2 The cervix

Labour induction and preparedness of labour induction can be implemented via pharmacological, surgical, and mechanical methods. The method is chosen based the condition of the cervix at the start of induction (1, 18).

The cervix is initially a solid, long, and closed organ, but undergoes remodelling as the gestation goes. The process of the cervix remodelling can be described in four phases: softening, ripening, dilation and lastly, repair after delivery. The first phase, softening of the cervix, is time-consuming and may start already during the first trimester of pregnancy. During this phase, tissue tensile strength in the cervix declines, making it softer. When the cervix has softened, the phase of cervical ripening takes over. Cervical ripening is a complex process happening in the weeks leading up to spontaneous labour and delivery. It has been defined as the peak of cervical tissue loss of tensile strength and structure. This is an important process where the cervix, among other things, shortens in length. Ripening is necessary for the cervix to be able to dilate in response to uterine contractions. The cervix is considered fully dilated at 10 cm (16, 19, 20).

#### *1.1.2.1 The Bishop score*

The Bishop score can be used to evaluate the condition of the cervix. The Bishop score is a scoring system named after Edward Bishop who set forth criteria for elective labour induction in 1964. The scoring system ranges from 0 to 13 points and is used to evaluate the cervix and define women likely to have a successful labour induction. The score is based on the patient's cervical dilatation, position, effacement, consistency of the cervix and foetal station. A widely used modified Bishop score takes only into account dilation, effacement and station and the scores range from 0 to 9. In the modified version, a Bishop score of 5 or less is considered as a unfavourable cervix, while a score of 6 or more indicates a favourable cervix (21).

If the cervix is unfavourable prior to labour induction it must be ripened using prostaglandins, a Foley or balloon catheter or oxytocin. If however the cervix is favourable, labour can often be induced solely with oxytocin (1, 18).

### 1.1.3 Prostaglandins

During labour, the body naturally produces prostaglandins to help and prepare the cervix in ripening. When labour is induced and the cervix is still unfavourable, synthetic prostaglandins can be given to help the process of ripening the cervix before giving drugs that produce contractions (22, 23).

Prostaglandins were first used for cervical ripening in the 1970s (22) and are available in many preparations (1). Initially, prostaglandin F2a was used, then prostaglandin E2 and analogues were developed and most recently there has been an increase in the use of prostaglandin E1 analogues, also named misoprostol. Prostaglandins can be administrated by various ways, i.e. orally, intramuscularly, intravenous, or using local administration via gel, vaginal tablets, suppositories or pessaries. Possible side-effects of prostaglandins include gastrointestinal symptoms, fever and uterine hyperstimulation (22).

### 1.1.4 Foley/balloon catheters

Intracervical balloon catheters are frequently used to mechanically ripen the cervix. Single balloon catheters are called Foley catheter, but double balloon catheters are also used to ripen the cervix. A double balloon catheter applies more pressure and has therefore greater utility in cervix ripening. A Foley catheter is on the other hand a great deal cheaper and has a shorter time range from insertion to delivery (24).

Balloon charters use mechanical pressure by inflating the balloon with sterile water, which leads to the release of prostaglandins in the body (25).

Foley/balloon catheter have a lower risk of uterine hyperstimulation and uterine rupture than prostaglandins and have therefore been recommended for women who have previously delivered via caesarean section (1, 26).

### 1.1.5 Oxytocin

Oxytocin is, as well as prostaglandins, released into the expecting mothers blood circulation. During labour the oxytocin peptide helps stimulate uterine contractions. When spontaneous labour is initiated, uterine sensitivity to oxytocin increases rapidly (4). Synthetic oxytocin is effective in increasing the frequency and intensity of contractions during labour and can hence reduce labour duration (27). It is the commonest induction agent worldwide and can either be used solely or in combination with other drugs or ripening methods (1, 18, 28). The drug has been designated as a high-alert medication in the United States, and great caution should be made when administrating oxytocin. Being a high-alert medication means that there is a heightened risk of causing significant patient harm if used incorrectly (4). A possible side effect of oxytocin infusion is tachysystole, excessive uterine activity defined as >5 contractions in 10 minutes averaged over 30 minutes. During contractions, blood flow to the foetus is reduced by approximately 60%. Under normal circumstances, the foetus is not harmed by the reduced blood flow, but it can be harmful if there is excessive uterine activity over a long period. Tachysystole can therefore, among other things, lead to hospitalization in the neonatal intensive care unit (NICU) (4).

The results from a Cochrane review comparing the use of oxytocin alone to expectant management, showed a higher rate of failed vaginal deliveries in the oxytocin group and conducted that oxytocin induction may increase the rates for interventions in labour. However, there was a higher rate of deliveries within 24 hours among women receiving oxytocin compared to expectant management (1, 18, 28). Recently, there have been discussions on whether the infusion of oxytocin should be discontinued during the active phase of labour (27, 29, 30). In France, the STOPOXY trial is in progress where women are randomized into two groups before they reach 6 cm dilatation. Oxytocin is then either continued or discontinued. Doing this, authors are anticipating seeing an improvement in child and maternal health if oxytocin is discontinued. This is based on the assumption that when women enter the active phase of labour, from 6 cm cervical dilatation, natural oxytocin takes over from the synthetic oxytocin. Discontinuing of oxytocin at this stage should therefore reduce exposure duration and the possible risks associated, including NICU hospitalizations (27). The CONSIDOX trial is also exploring the effects of discontinuing oxytocin use in the active phase of labour. The trial aims to investigate the effect of oxytocin simulation in relation to caesarean section rates after labour induction in Denmark and the Netherlands. A pilot study from Denmark showed that the group where oxytocin infusion was discontinued had fewer cases of uterine tachysystole and non-reassuring foetal heart pattern (29). A study from 2015 found that the total duration of labour, and the total oxytocin dose was significantly less in the group where oxytocin infusions were discontinued during the active state of labour compared to the group receiving oxytocin until delivery (30).

### 1.1.6 Membrane sweeping

Membrane sweeping is not formally regarded as a type of induction, but as an intervention that aims to reduce the need for formal labour induction (3). Membrane sweeping is a mechanical technique used to detach the inferior pole of the membranes from the uterine segment. Doing this produces prostaglandin hormones that encourage effacement and dilatation potentially promoting labour. (16, 18, 31). Membrane sweeping is a low-cost procedure and can be performed without the need for hospitalisation and is hence suitable for non-urgent cases. The procedure can be uncomfortable for the expecting mothers and is only possible to perform if the cervix has begun to dilate (31).

### 1.1.7 Artificial rupture of membranes, amniotomy

Membranes can also be ruptured artificially, this process is also called amniotomy. Amniotomy can be done with an amnihook, where the hook is used to tear apart the membranes. Amniotomy is done in order to increase the production and release of prostaglandins and oxytocin, hence stimulating and shortening the length of labour (1).

A Cochrane review including 5,583 women in 15 studies comparing women intended to preserve the membranes to women undergoing routine amniotomy did not find a statistically significant difference between the groups in length of the first stage of labour (32).

### 1.1.8 What is the best method?

As seen in the discussion above, there are multiple methods used for cervix ripening and labour induction, even more than have been covered here. In addition, combinations of different methods have frequently been used in order to achieve successful induction of labour.

Despite numerous studies trying to find the most ideal labour induction agent, one who decreases time to delivery and does not increase maternal or neonatal adverse outcomes, a preferred agent has not yet been identified. Claims have been made that there is not one perfect agent for all, and therefore a medical decision must be made on a case-by-case basis. Practices have been recommended to take previous obstetric history of the expecting mother into account when choosing labour induction methods (4, 33).

## 1.2 Labour duration

There is no standardized or universal definition on what the normal progress and duration of labour is. This is partly due to the complexity of labour onset making it difficult to distinguish between phases, and the fact that the division between phases can only be determined after the delivery is complete (34). Studies define labour onset in various ways, and a systematic review found that among 62 studies on labour onset four definitions of labour onset were used: latent phase, active phase, first stage and unspecified labour. Only 40% of the included studies used evidentiary basis for the definition of labour onset, and little consensus was between definitions, even when studies were referring to the same stage or phase of labour. The most common indicators for labour onset were cervical dilatation and regular painful contractions (35).

### 1.2.1 Stages of labour

Despite of this lack of standardized definition, labour is divided into three stages. The first stage is often defined as the time from labour onset to full cervix dilatation. This stage is divided into two phases, the "latent phase" and the "active phase". During the latent phase, the cervix shortens in length and the phase is usually defined as the period from beginning of regular contractions and until a certain number of centimetres in dilatation has been reached (16). Traditionally, the latent phase has been identified from 0 – 4 cm dilation, but a more modern labour curve identifies it from 0 – 6 cm of cervical dilation (36). It can be difficult to estimate the duration of the latent phase, but it has been stated that the phase usually lasts between 3 and 8 hours (16). The active phase is the time from the end of the latent phase and until full dilatation of the cervix. It is often considered abnormal if the dilatation during the active phase is less than 1 cm in two hours. This phase is also variable in duration, often lasting between 2 and 6 hours. The mean duration is shorter in multiparous women than primipara women in the active phase (16).

The second stage of labour can be defined as the duration from full cervical dilation and to delivery of the foetus. This stage is often divided into the "passive phase" from full dilatation till the onset of involuntary expulsive contractions, and the "active second stage". During the active second stage, the head of the foetus is low in the pelvic floor, and the mother gets the urge to push. If the urge of involuntary pushing does not happen, the distinction between the two phases is made when the midwife directs her to make pushing efforts. The second stage of labour should preferably not last longer than 1 hour for multiparas and no longer than 2 hours for primiparas (16).

The time from delivery of foetus and until the placenta and membranes have been delivered is the third stage of labour. This stage should under normal circumstances not last longer than 30 minutes. The average duration from labour until delivery is 5 hours for multiparas and 8 hours for primiparas (16).

### 1.2.2 Duration of labour induction

As with the normal progress of labour, there is no generally accepted definition of failed induction of labour. Many definitions of failed induction have been used by studies, for example, failed vaginal delivery, women not entering the active labour phase and failure of labour after using a certain number of ripening agents (37). An American study comparing labour progress in women undergoing labour induction and women who laboured spontaneously found that the total labour time was significantly longer among women undergoing labour induction. The median labour duration among primiparas undergoing labour induction was 5.5 hours, compared to 3.8 hours among those having a spontaneous labour. The median duration among multiparas was 4.4 hours among women having their labour induced while it was 2.4 hours among those having a spontaneous labour. Further analysis showed that the difference in duration between the two groups was in the latent labour phase. When the women where in active labour however, the median time to dilate 1 centimetre was similar when the groups were compared (14). It has also been shown that women undergoing elective labour induction at 39 weeks' gestation have an increased time from hospital admission to delivery compared to women having their labour induced based on medical reasons, but there was however seen an decrease in the delivery to discharge time, both among primiparas and multiparas (38). Elective labour induction has also been found to affect the labour duration, as a study by Dögl et al. (2018) noted. The study found a higher proportion of deliveries within 24 hours after labour induction among women having their labour induced based on medical reasons compared to elective induction (15).

A recent Australian study reported that the initial vaginal examination prior to induction of labour did not appear to be associated with the duration of labour. A favourable cervix 12 hours after the start of labour induction did seem to be the most predictive factor of delivery duration (39). Rane et al. (2005) measured the cervical length pre-induction and found that it had an significant association with the labour duration in women who had their labour induced. They also found that parity, gestational age, and birth weight were significant factors in predicting whether delivery had been completed within 24 hours of induction (40).

There are not many studies available on the effects of labour induction duration on infant outcomes following birth. Blackwell et al. (2008) did study this relationship using data from 2005 in Michigan, USA. Infants in the study were divided into three groups, based on labour induction duration; <24 hours, 24-48 hours and >48 hours. Of infants born after a labour induction lasting <24 hours, 1.3% were admitted to the NICU, compared to 1.2% of infants born after a labour induction lasting 24-48 hours and 1.0% of infants born after a labour induction lasting < 48 hours. The study did not find a relationship between induction to delivery time and adverse neonatal outcomes, including admissions to the NICU (41). Cheng et al. (2009) studied the association between the length of the first stage of labour and perinatal outcomes in San Francisco from 1985-2001. The first stage was defined as onset of painful, regular contractions, every five minutes or at least 3 contractions in a ten-minute period and the stage ended at complete cervical dilation. The authors did not stratify the cohort by parity or induction methods, as they did not observe large differences in perinatal outcomes based on these factors. The first stage of labour lasted between 0-12 hours among 71.9% of participants (n=593) and only 5.0% (n=181) of the expectant mothers experienced the first stage of labour lasting longer than 24 hours. The study found that a progressive length of the first stage of labour among women undergoing labour induction was associated with an increased risk of NICU admissions. Analysis where the group of women with the first stage of labour lasting 0-12 hours was the reference group showed adjusted OR of 1.08 (95% CI 0.66 -1.62) for the group of first stage lasing 12-18 hours, 1.76 (95% CI 1.00-3.09) for the group of first stage lasting 18-24 hours and 2.03 (95% CI 1.10-3.74) for the group with the first stage of labour lasting 24 hours or more (42).

## 1.3 Indications for labour induction

There are many possible reasons for the need of labour induction. Here, some of the most common indications for labour induction will be reviewed with reference to existing knowledge.

### 1.3.1 Preeclampsia, eclampsia

Hypertensive disorders of pregnancy can have serious effects on mother and foetus. Preeclampsia is defined as the onset of hypertension developing >20 weeks of gestation, accompanied by proteinuria or evidence of end-organ dysfunction. Preeclampsia seems to be caused by abnormal placentation followed by a dysfunctional maternal immune response. Risk factors for preeclampsia include for example chronic hypertension, diabetes, nulliparity, BMI >30 $kg/m^2$, race and previous history of preeclampsia. The definite treatment of preeclampsia is delivery, and women ≥37 weeks of gestation are advised to have their labour induced (43).

Eclampsia is defined as seizures in a pregnant woman with preeclampsia with no other identifiable cause. The underlying mechanism causing the seizures is not well understood (43).

Studies have not provided agreeing results on when induction of labour should be carried out for women with hypertensive disorders, but some indicate that it should be done between weeks 38 and 39 of gestation in order to minimise maternal and neonatal morbidity (44).

### 1.3.2 Other hypertensive disorders

Other hypertensive disorders can have great effects on pregnancies. The rate of chronic hypertension during pregnancy is expected to rise parallel to an increase in the prevalence of obesity and higher average maternal age. Chronic hypertension is diagnosed in women having hypertension before conception if the blood pressure elevates prior to 20 weeks of gestation or if the hypertension lasts more than 12 weeks beyond delivery (43).

Gestational hypertension is defined as hypertension developing after 20 weeks of gestation or more in women not suffering from hypertension prior to gestation. The rate for gestational hypertension is higher among nulliparous women than multiparous women (43).

The severity of the blood pressure elevation, both in chronic hypertension during pregnancy and gestational hypertension can have strong effects on a range of factors affecting both mothers and infants. Mothers with severe chronic hypertension or gestational hypertension are in risk of delivering prematurely, having small infants, as well as being at great risk of developing preeclampsia (43).

### 1.3.3 Diabetes

Diabetes is a metabolic disorder characterised by an autoimmune process destroying insulin producing beta cells of the pancreas. Diabetes is often divided into type 1 and type 2 diabetes. Type 1 diabetes usually occurs early in life while type 2 diabetes develops later in life and is related to lifestyle. The prevalence of type 2 diabetes among younger individuals is rising (45). The incidence of diabetes diagnosis among expecting mothers in Iceland increased from 0.5% in 1995-1999 to 4.8% in 2010-2014 (46). Diabetes type 1 and type 2 have been associated with increased adverse neonatal outcomes, for example foetal macrosomia, preterm birth, preeclampsia, increased risk of stillbirth and admissions to the NICU (45).

Gestational diabetes is diabetes diagnosed in the second or third trimester of pregnancy in women that did not have diabetes prior to gestation. As with diabetes, the prevalence of gestational diabetes is on the rise, but the prevalence varies depending on population characteristics and the diagnostic criteria used. Major reasons for increased prevalence in gestational diabetes include increasing obesity, physical inactivity and rising maternal age. Treatments aim at reducing the risk of associated adverse pregnancy outcomes. This includes a healthy diet, blood glucose monitoring and possibly insulin therapy (47).

In Iceland, women with known risk factors for diabetes are screened for diabetes type 2 and gestational diabetes in the first antenatal care visit, and again at week 24-28 of gestation. In some cases a dietary change and increased exercise is sufficient, but those with more severe diabetes get insulin therapy and are classified as high-risk pregnancies (48).

### 1.3.4 Obstetric cholestasis

Obstetric cholestasis, also called intrahepatic cholestasis of pregnancy, is a liver disease typically occurring during the third trimester of pregnancy. The disease causes abnormal liver function and raised levels of bile acid. The main, and sometimes the only, symptom is pruritus, usually in the palms and soles, but it may occur anywhere. Obstetric cholestasis has been associated with negative pregnancy outcomes, including non-reassuring foetal status, NICU admissions and stillbirth. The incidence varies among ethnicities and geographic locations and is in some counties more common during winter, when natural selenium levels and vitamin D levels are lower. Higher rates of gestational diabetes and preeclampsia have been reported in women suffering from obstetric cholestasis. Due to studies showing increased risk for adverse neonatal outcomes labour is sometimes induced in women with obstetric cholestasis (49). The systematic review by Coates et al. (2020) found mixed evidence on the possible benefits of inducing labour in case of obstetric cholestasis (44).

### 1.3.5 Prolonged pregnancy

A delivery between 37 and 42 weeks of gestation, equivalent to 259 to 293 days measured from the first day of the last normal menstrual period, are classified as term deliveries (50). In 2008 the National Institute for Health and Clinical Excellence published recommendation stating that women with uncomplicated pregnancies should usually be offered labour induction between weeks 41+0 and 42+0 of gestation (51). These recommendations are still relevant, and labour induction is recommended if it is certain that the expecting mother has reached 41 weeks of gestation (1). This is due to an increase in adverse perinatal outcomes after 40 weeks of gestation, and a significant increase post-term (≥ 42 weeks of gestation). This became clear in the Swedish study SWEPIS (Swedish post-term induction study), aiming at inspecting whether induction of labour at 41 weeks of gestation would improve perinatal and maternal outcomes compared to expectant management and induction of labour at 42 weeks of gestation. Due to ethical reasons, the study came to an end before planned as there was a statistically higher perinatal mortality in the expectant management group (52). This is similar result as was found in a Cochrane review from 2018 including 30 randomised controlled trails. The review compared two policies, labour induction at or beyond term (usually >41 weeks of gestation) versus expectant management (53). There were fewer perinatal deaths and stillbirths where labour induction was performed at or beyond term compared to expectant management. There were also fewer caesarean sections in the labour induction policy group, but a higher rate of operative vaginal births. The rate for NICU admissions was lower in the labour induction groups. The evidence for all of these events were moderate-quality (53). The review was updated in 2020, where 34 RCTs were included. The results for the updated review were the same as in the earlier one, there were fewer perinatal deaths, fewer caesarean sections and lower NICU admission rates were observed in the labour induction group, compared to expectant management (54).

A Danish systematic review from 2018 compared outcomes of labour induction at 41+0-6 weeks of gestation to 42+0-6 weeks of gestation. The review found an increased risk of a number of adverse outcomes including caesarean section and uterine rupture when labour was induced at 41+0-6 weeks of gestation. The data could not draw conclusions on perinatal death, as it lacked statistical power. The authors did therefore not recommend labour induction prior to post-term and noted that 70% of the women in the group of non-induced women went into spontaneous labour (55). The effect of labour induction during gestational week 41 has been studied in Iceland, using data from the Icelandic Medical Birth Registry during 2013-2016 (56). The study compared women with a spontaneous labour to women who had a labour induction. The indicators for infant outcomes were Apgar scores, meconium staining and foetal distress. The study did not report a statistically significant effect of labour induction on these variables (56).

## 1.4 Elective labour induction

As mentioned above, the WHO´s recommendations state that induction of labour should only be performed when there is a clear medical indication for it (3). When labour induction is performed without a clear medical rationale being present, it is called elective labour induction (4).

In 2019 the American Congress of Obstetricians and Gynaecologist (ACOG) reiterated their recommendations of labour induction for non-medically induced induction from 2009 and 2013, stating that elective labour induction should not occur prior to 39+0 – 39+7 weeks of gestation (57). ACOG has also stated that labour induction may be induced for logistical reasons, for example if the woman lives a long distance from the hospital or has a history of rapid labour (58). It can be problematic to estimate the rates of elective induction accurately as it depends on what is categorized as elective by each institution. This opinion may differ between guidelines, hospitals and even between maternity care providers within the same hospital (59). A recent Norwegian study identified the rapid increase in elective induction to be the outcome of multifactorial changes, including better induction methods and more liberal induction. It is also suggested that patient empowerment may contribute to the increase, with an improved ability to plan the timing of delivery (15).

In Norway, one in ten labour induction were conducted without medical indication, making it the third most common reason for labour induction in term pregnancies (15). A French study found the elective induction rate to be about 14% in 2010. Among the elective labour induction 47% were performed on maternal request. The study did find that private maternity units and units performing fewer than 1,500 deliveries per year performed more elective induction (60).

In 2018 the results from a large, randomized trial, A Randomized Trial of Induction Versus Expectant Management study, or the ARRIVE trial, where published (11). The trial aimed at shedding light on the effects of labour induction between gestational age 39 weeks 0 days to 40 weeks 6 days. Expecting primipara women were randomly assigned to either labour induction (performed between 39+0 to 39+4 weeks of gestation) or expectant management (until 41+0 weeks of gestation). The trial did not find a statistically significant difference in admissions to the NICU between the two groups, RR 0.90 (95% CI: 0.79-1.03). Women in the induction group were significantly less likely to have hypertensive disorders of pregnancy and reported less pain and more control during the delivery. Women and infants assigned to the labour induction group did spend more time in the labour and delivery unit but went home from the hospital earlier postpartum than the women and infants in the expectant management group. The study reported a significantly lower frequency of caesarean delivery in the induction group (11). The ARRIVE trial may have the potential to change current practice. The first step may have already been taken as the ACOG has published a Practice Advisory stating that labour induction at 39 weeks of gestation is a reasonable option in low-risk primipara mothers after the publishing of the study results (61).

A meta-analysis consisting of six studies compared elective induction of labour at 39 weeks and expectant management found that an elective induction of labour at 39 weeks was associated with a lower frequency of caesarean delivery (12). Infants born to mothers in the induction group were also less likely to be admitted to the NICU compared to infants in the expectant management group (12). A systematic review by Saccone et al. (2019), reported that there was not an association between labour induction at 39+0 to 39+6 weeks of gestation and increased risk of caesarean delivery. One of the secondary outcomes in the review was NICU admissions, but there was not found a statistically significant difference between women undergoing elective induction and those managed expectantly until weeks 41-42 of gestation (62).

Souter et al. (2019), did also report a decrease in caesarean births among primipara mothers having an elective labour induction at 39 gestational weeks compared to expectant management. They did however find a similar caesarean birth rate among multiparas having their labour induced and on-going pregnancies. This study also reported a decrease in pregnancy-related hypertension both in primipara and multipara mothers undergoing elective induction of labour and a statistically significant decrease in NICU admissions among primiparas induced at 39 weeks of gestation (38).

A study by Ekéus and Lindgren (2016) showed other results. Their study was conducted in Sweden during the years 1999-2012 and included 1,078,536 women giving birth at term. This study did not only include women undergoing elective induction, but special notice was made that almost half of the induced population did not have a medical complication documented. The authors found that induced labours were associated with 2-3 times greater risk of an unplanned caesarean section, with the exception of multiparas in gestational week 37-38 (8).

A large retrospective cohort study in Scotland during the years 1981-2007 including 1,271,549 women carrying singleton infants born at term (gestational age >37 weeks) compared women undergoing elective induction to women treated with expectant management (13). The study found that elective induction at term did increase the NICU admission rate among infants, but that the elective induction can reduce perinatal mortality. They did not find a strong association between elective induction and increased odds of caesarean section (13).

In the Netherlands, the INDEX study was conducted during the years 2012-2016 (63). The aim of the study was to compare labour induction at 41 weeks of gestation with expectant management until 42 weeks of gestation in relation to perinatal mortality and neonatal morbidity. The study did observe chances of good perinatal outcomes for both groups, with a slightly better outcome for infants born after labour induction. Among infants in the induction group, using intention-to-treat analysis, 0.3% were admitted to the NICU, and 6.6% were admitted to medium care. The rates in the expectant management group were 0.9% NICU admissions and 6.7% for medium care. Mode of delivery was a secondary outcome in the study, but no significant difference was found in caesarean section between the groups (63).

In Norway, the rates for elective induction versus medically induced labours was investigated in comparison to parity. It was seen that elective induction was more common among multiparas than primiparas (15). This was also seen in the population based France study, where the adjusted OR for elective labour induction was 4.7 (95% CI 3.1; 7.2) for multiparas compared to primiparas (60).

The studies referred to above do for the most part compare elective induction in gestational week 39 to expectant management (11, 12, 38, 62). The study by Ekéus and Lindgren (2016) was the only one showing a definite higher caesarean rate among women undergoing labour induction, and this is also the one study not comparing labour induction to expectant management (8). The studies are not as congruent when it comes to infants' risk of being admitted to the NICU after elective labour induction. One study found an increased NICU admission rate among infants born after labour induction (13), two did not find a difference (11, 62), while three studies found a decreased risk for NICU admissions (12, 38, 63).

## 1.5 Labour induction in Iceland

Shifting the focus to labour induction in Iceland, it is important to keep in mind that there can be fluctuations between years due to a small number of births each year (5). The maternity ward at Landspítali makes use of performance metrics, in order to monitor various aspects of the activities performed at the unit (64). The activities are identified from ICD-10 codes. The metrics are updated weekly and are used to categorize the results from the activities into optimal performance, acceptable performance and unacceptable performance. The categorisation is under constant development as new evidence appears. In 2016, the optimal rate for labour induction was 0.0-19.9%, acceptable rate was 20.0-24.9% while an unacceptable rate of labour induction was 25.0-100% (64). Icelandic guidelines indicate that labour should be induced when gestational age has reached 41 to 42 weeks of gestation. Mothers over forty years old are recommended to have their labour induced from week 40 to week 41 of gestation (65).

The Icelandic Medical Birth Register does not register the induction method or direct indication for each delivery, however, ICD diagnoses codes for complications during pregnancy and delivery are registered. Maternity registers have also been viewed in order to find the direct indications. This was done in an Icelandic study in 2013, where the author analysed all maternity registers from the National University Hospital of Iceland, Landspítali, in March 2012 with regards to induction method and induction indications (66). A total of 231 women delivered during the month. The majority of labour induction, 54.8%, were conducted via the prostaglandin Cytotec (misoprostol). The second most common labour induction method was artificial rupture of membranes, performed on 25.8% of the women. The oxytocin drug Syntocinon was used in 14.5% of cases and catheters were used in 3.2% of the cases. The induction method was not registered in 2.0% of the induction during March 2012. The study points out that rules for procedure were changed the year 2008 at Landspítali, where Misoprostol was being used instead of dinoprostone. The most common indications for labour induction were prelabour rupture of membranes (PROM), 22.6%, gestational age, 19.4% and preeclampsia/hypertension, 17.7% (66). PROM is the rupture of foetal membranes prior to the onset of labour. PROM at term is defined as rupture of membranes at least one hour prior the onset of uterine contractions (67). A delay in the onset of labour after the rupture of membranes increases the risk for neonatal and maternal infections. It is therefore common to induce labour if labour has not started within 24 hours of membranes rupture (16, 67). In 4.8% of labour induction in Landspítali in March 2012, the induction indication was not registered. The authors concluded that about 6.5 – 13.5% of labour induction during March 2012 were elective labour induction. The author called for better registration of indication for induction and for better coordination in registrations (66).

The birth registration report from Iceland in 2018 found that the vaginal birth rate was slightly lower among women undergoing labour induction, compared to women having a spontaneous labour (5). The report also noted an increase in caesarean sections among primipara mothers who had their labour induced following a new labour induction method, oral intake of misoprostol pills. The caesarean rate among multiparas was low. The report also noted a general increase in labour induction and indicated that the increase goes hand in hand with increased risk-related factors among women giving birth, including gestational diabetes, obesity, and advanced age. It is also noted that new protocols e.g. in treatment of women with hypertension, preeclampsia and gestational diabetes have increased the number of women undergoing labour induction (5). An Icelandic study from 2018, compared births in Iceland from 1995-1999 to births from 2010-2014 (46). They observed an increase in labour induction both among primiparas and multiparas. This study did however not find the increase being the results of changes in mothers sociodemographic characteristics nor by increasing diagnoses of common pregnancy-related conditions. The study found that the rising induction of labour rate was most notable among women without a diagnosis of hypertensive disorders or diabetes (46).

## 1.6 Elective caesarean sections

A global increase in elective caesarean sections has been identified in the academic literature. A study including approximately 98.4% of all births in the world, showed that the caesarean birth rate almost doubled over a fifteen-year period, as caesarean sections made up 12.1% of all birth in 2000 compared to 21.1% of births in 2015 (68). The increase is believed to be caused both by an increase in births occurring in health facilities, as well as an increase in caesarean sections within health facilities. In Western Europe, the caesarean section rate in 2015 was 19.6% (68), but the Nordic countries have the lowest caesarean rates globally (69). Just as with labour induction, the WHO does not recommend performing an caesarean section when there is not a medical indication for doing the procedure (70). WHO states that populations should not have a caesarean rate higher than 10-15% of births, as surgeries are associated with both short and long-term risk, possibly affecting both the mother and the infant (70). In NICE guidelines on caesarean birth, there is emphasis on informing expecting mothers on risks and benefits of caesarean section in order to support them in making informed decisions regarding the delivery (71). In Iceland, elective caesarean sections are defined as caesarean sections that were planned at least 8 hours prior to the operation and are performed during work hours (5). The classification may however differ between countries (69).

The mean elective caesarean delivery rate in Europe 2015 was 11.3% but the rate ranged from 3.6% to 40.5% between countries (69). The caesarean section rate among all births in Iceland in 2018 was 16.1% (n=672), and elective caesareans accounted for 6.7% (n=277) of births (5).

A recent systematic review of prospective studies on the outcomes for planned caesarean sections versus planned vaginal delivery weeks concluded that there is need for a standardised core outcome set for planned delivery in order to enable better comparisons of outcomes following planned deliveries (72). Among studies that have researched the association between elective caesarean sections and planned vaginal delivery in relation to neonatal outcomes is a study from Sweden, including primipara mothers. The study did not find an association between the delivery modes and NICU admissions. The study only included women planning a delivery by caesarean section because of breech presentation or maternal request (73). Planned caesarean sections among primipara mothers was however linked to decreased risk of NICU admissions in a study by Geller et al. (2010). The study analysed data based on planned route of deliver prior to onset of labour, but not the actual route of delivery. The overall NICU admission rate in the study was 6.6%. The odds for NICU admission were still significantly higher among infants born associated with planned elective caesarean delivery after adjustment for possible confounders (74).

## 1.7 Monitoring after birth

The first neonatal intensive care units (NICUs) in America were established in 1960, and since then the neonatal mortality rate has fallen greatly as a result of specific interventions and specialised care for prematurely born and sick infants (75). The American Academy of Paediatrics (AAP) divides the neonatal care into four levels, based on the severity of care needed (75). Most infants are admitted to the NICU based on low birth weight and low gestational age (76). Neonatal respiratory disorders is the most frequent reason for NICU admission immediately after birth. When labour does not occur naturally, which is often the case when labour is induced and in elective caesarean sections, the infants are often less developed and are hence more physically vulnerable compared to infants born after spontaneous labour (77). Infants born to primipara mothers are more likely to be admitted to the NICU, than infants born to mothers who have previously given birth (76). When studying NICU care, Braun et al. (2020) emphasise the importance of studying the whole population at risk, namely, both infants admitted to the NICU and infants who only require rooming-in-care with their mothers in order to get a holistic view of the infants needing monitoring following birth (76).

During the years 2007-2012 NICU admission rates increased in USA. Analysis showed that there was increased probability for US infants at all birth weights to be admitted to the NICU, also after adjustment for infant and maternal risk factors. During the study period from 2007-2012, infants admitted to the NICU were increasingly likely to be born at term and have a normal birth weight (75). These results were however contrary to the results of Braun et al. (2020) who looked at the period from 2010-2018 in Southern California. This study found a decrease in NICU admissions as well as number of NICU patient days. Most of the decrease in NICU admissions was associated with the decrease in admissions among infants with gestational age >34 weeks and birth weight 2000 g or more (76).

In the United States, a significant variation in admission rates has been observed between NICUs, and within individual NICUs, among infants admitted without an identifiable cause. These infants had a shorter length of stay compared to infants with an absolute cause for admission, and it has been suggested that infants admitted to the NICU without identifiable causes may not have required admission to the unit (78).

NICU admission can have an effect on infant's psychosocial development and cognitive functioning (79). NICU admissions have also shown to be hard on mothers, and the separation from the new born infant can affect the mother-infant bonding, be stressful and emotionally draining (80). Healthcare personnel have important jobs of including caregivers in giving information and including mothers during the NICU stay (80). Infants' admission to NICU is also likely to affect the mother's partner. Studies among fathers have shown that they often are stressed during the NICU admission period and feel left out as health care personnel mainly focus on the mother and infants (81, 82). Family-centred NICU care that incorporates parents in decision making on the infant's care and empowers parents is important for optimal outcomes for infants and parents (79).

### 1.7.1 Labour induction and monitoring after birth

As previously mentioned, Cochrane reviews have found evidence for lower NICU admission rates among full-term infants born after labour induction compared to expectant management (53, 54). A population-based study from Austria did however find that labour induction was associated with increased odds of adverse neonatal outcomes, one of them being NICU admissions (83). The study included all singleton births except primary caesarean sections in Austria from 2008-2014. The labour induction rate was 19.7%. Odds for admission to the NICU were significantly higher for infants born after labour induction compared to spontaneous labour at all gestational age weeks. After adjustment for potential confounders, the OR for NICU admission was still higher among infants born after labour induction, adjusted OR 1.41 (95%CI 1.31; 1.51) (83). This was also the results from a study carried out in Switzerland. This study did separate analyses for primipara mothers and multipara mothers, and the risk for NICU admission was higher for infants born after labour induction, both among infants born to primipara mothers (OR 1.39 (95%CI 1.15; 1.69)) and infants born to multipara mothers (OR 1.51 (95%CI 1.15;1.90)) (84).

### 1.7.2 Elective deliveries and monitoring after birth

Elective caesarean sections and elective labour induction are often classified together as elective deliveries. The classification is not always consistent between studies, and Teitler et al. (2019) classified elective deliveries as caesarean deliveries with no trail of labour, caesarean deliveries following induction and induced vaginal deliveries. These delivery methods were compared to noninduced vaginal deliveries among 150,032 births in New Jersey giving birth in 1997-2007. Women having singleton first births were included, as well as multipara mothers given that their first labour was a vaginal delivery. This criterion was included as having a caesarean section delivery increases the likelihood of having caesarean section in later births. If labour was induced based on medical reasons according to the ICD-9, as well as births with a gestational age of 41 were excluded from the study. They found that the elective deliveries rate more than doubled during the study period. The authors found a statistically higher risk for NICU admission among infants born after labour induction (OR 1.15 (95%CI: 1.04; 1.28), caesarean deliveries with no trail of labour (OR 2.13 (95%CI: 1.91; 2.38) and caesarean deliveries following labour induction (OR 2.54 (95%CI 2.36; 2.75), when noninduced vaginal deliveries were the reference category. The study also found a statistically significant higher neonatal hospitalization costs when deliveries were elective compared to spontaneous labour. The study found that each additional week of gestation decreased the odds of NICU admissions. This is interesting in the light of changes in current practice where labour induction is stated as a reasonable option to induce labour at 39 weeks in low-risk primipara mothers (85).

Dunne et al. (2009) studied neonatal outcomes of elective labour induction, elective caesarean sections and spontaneous labour among full-term pregnancies at a London hospital, from 1996-2005. To be included in the study, the pregnancy had to be low-risk, excluding all women with any medical or surgical complication of pregnancy. This resulted in a study population of 9,686 women. Contrary to Teitler et al. (2019), the study did not find statistical differences in NICU admissions among the delivery groups. The analysis was made both for nulliparous and multiparous mothers, and no associations were found, nor was there an association between the delivery groups and NICU triages (59).

### 1.7.3 Labour induction indication and monitoring after birth

De Vires et al. (2019) sought to study the outcomes of induction of labour in Sidney, using data from nulliparous women, carrying singleton infants, who had their labour induced at 38 or 39 completed weeks of gestation in 2009-2016. The study found that labour induction was associated with higher risk of NICU admissions, compared to spontaneous labour. Of the 3,330 undergoing labour induction, the most common indication was spontaneous rupture of membranes, clear liquor (n=829), followed by gestational diabetes (n = 789). There were 37 women who had their labour induced based on maternal choice. The induction indication with the highest NICU admission rate was mothers pre-excising diabetes, where 44% of infants were admitted to the NICU following birth. This indication had a notably higher NICU admission rate than other indications, as the second highest NICU admission rates were 11%, where labour was induced because of suspected foetal compromise, reduced foetal movements or antepartum haemorrhage (86). Gerli et al. (2013) study from Italy found that the most common indications for labour induction among primiparas was prolonged pregnancy where the gestational age was 41+1 weeks or more, 27.0%, while it elective induction was the most common indication for induction of labour among multipara mothers, 31.6% (87).

### 1.7.4 Monitoring after birth in Iceland

Great progress has been made in reducing neonatal mortality in Iceland. At the start of the 20th century 60 out of every 1000 infants died during the first month of life, but the rate had been reduced to 20 out of every 1000 by the mid 20th century (88). In 2018, the infant mortality in Iceland was 1.42 in every 1000 births, and Iceland is among the countries with the lowest neonatal mortality globally (5). Prior to 1930 most women in Iceland gave birth at home, but there were some small maternity homes for women who could not deliver in their homes for some reason. In 1930, major maternity homes were established, midwives and physicians supervised these homes. In 1949 the maternity at Landspítali, the National University Hospital of Iceland, was enlarged from 17 to 60 hospital beds. Women living in the area were encouraged to give birth there (89). In 1976 a NICU began operating at Landspítali were premature and sick infants can get special monitoring under the supervision of midwives, nurses and paediatricians and other healthcare personnel (88). Landspítali is by far largest birthplace in Iceland. In 2018, 74% of all births in the country were at Landspítali (5). The NICU at Landspítali is the only unit in Iceland with a practicing neonatal physician so all premature infants with gestational age <34 weeks should be cared for at Landspítali, this also goes for infants with known serious defects or problems (5). Around 400 infants are admitted to the NICU yearly, and almost 700 infants used the day unit. About 40%, of infants in the NICU are born prematurely (90). In Akureyri Hospital, there is a NICU with room for two infants, but the unit does not care for infants born prior to gestational week 34 (91). In 2018, 329 infants were born at Akureyri Hospital (5), 66 infants were admitted to further monitoring of which 53 were admitted to the NICU. The average length of stay among infants at the NICU was 3.3 days (91).

Landspítali does not use the distinction in four levels of units as the AAP, as there is only one unit for the whole country, but there are infants who do not require admission to the NICU but are instead monitored specially in the maternity ward. An Icelandic study from 2011 described infants' reasons and duration for triage admissions to the NICU among infants who were not admitted to the unit following the triage (92). Most infants had more than one reason for triage registered, but breathing problems was the most common reason (34.5%), followed by sluggish/weak infant and/or low Apgar score (10.2%) and caesarean birth (9.5%). The majority of infants admitted for triage were full term, as those with gestational age >35 weeks were immediately admitted to the NICU. The most common risk factors were mothers with gestational diabetes, infant growth restriction and risk factors following complicated births, especially assisted births. One third of infants admitted for triage were in the NICU for 2 hours or less. In light of the short triage duration, authors conclude that there may be reason to assess whether some of the infants could be monitored in the maternity ward, in order to avoid infants separation from mother (92).

## 1.8 Summary

There are certain risks linked to labour induction. Direct risks are the risks following the actual labour induction. These risks include for example tachysystole, uterine hyperstimulation and uterine rupture. It is also likely that the labour is being induced as the mother or infant are experiencing some of the indications mentioned above and are therefore in risk of developing adverse outcomes if the pregnancy is continued. Even though WHO states that there should be a medical indication for the labour induction, large recent trials have found evidence that labour induction in healthy women at term might have a positive impact on pregnancy outcomes. After the publishing of promising results in this regard, guidelines and practices are beginning to shift in a direction of more liberal use of labour induction. It can be hard to determine the absolute rate for elective induction, as it is in some ways a subjective evaluation.

With the advent of NICUs, the infant mortality rates have dropped drastically. Neonatal care providers are taking important decisions when deciding on whether to admit infants to the unit as it can have negative outcomes for infants and parents. Both foreign and domestic studies have questioned the high NICU admission rates among full term infants with normal birth weight.

Iceland is among the countries with the highest labour induction rates worldwide. It is therefore highly relevant to gain as much knowledge as possible on the rates of infant monitoring after birth according to onset of labour for the Icelandic setting.

# 2 Aims

The overall aim of this study was to examine whether there is a relationship between labour induction and the need for monitoring of infants in Iceland. Furthermore, the labour induction duration and the reason for the labour induction was examined in relation to infants need for monitoring.

Specifically, the aim was to study:

1) the frequency of infant monitoring for term singleton infants stratified by induction of labour, spontaneous labour or elective caesarean section

2) the rate of infant monitoring after birth according to the length of labour induction for term singleton infants whose birth had been induced

3) the difference in the rate of infant monitoring after birth by labour induction indication among term singleton infants whose birth had been induced.

# 3 Methods

## 3.1 Study population

This is a retrospective cohort study based on data from the Icelandic Medical Birth Register during the years 2009-2018. The study population was identified through the Icelandic Medical Birth Register. The registry is held by the Directorate of Health and stores various information on pregnancies, births, mothers and infants where gestational age was >22 weeks or the infant weighed >500 g (46, 93). The Icelandic Medical Birth Register has been operating since 1972 and has been electronic since 1981. The majority of the information comes from health care clinics, whilst a small part is registered at the women's health ward, Landspítali (93). The other Nordic countries hold comparable registries, and to facilitate cross-national comparison, the Icelandic Medical Birth Register registers information according to the recommendations of the Nordic Medico-Statistical Committee, the Classification of Surgical Procedures (NCSP), and the International Classification of Diseases, 10$^{th}$ revision (ICD-10) (46).

The dataset obtained for this study included data on births in Iceland from 1997-2018. Due to missing registration on infants need for monitoring after birth and labour onset during the first 12 years of the dataset, the present study included data from births over a 10-year period, from January 1$^{st}$ 2009 to December 31$^{st}$ 2018. Only liveborn singletons, born at term (37+0 – 41+6 weeks of gestation (50)) were included in this study to make the results more generalisable.

The original dataset contained information on 95,733 infants. After excluding infants born prior to January 1$^{st}$, 2009, 44,019 infants remained. Furthermore, 132 infants were excluded because of stillbirths, 1,363 infants were multiples, and 2,906 infants were not born at term, based on pregnancy ultrasounds. Furthermore 1,175 infants were excluded as they were missing other relevant information; 59 were missing information on labour onset and 1,116 were missing information on labour induction duration.

This resulted in a study population of 38,443 infants. Of those, 28,228 were born after spontaneous labour, 7,593 were born after labour induction and 2,622 were born after an elective caesarean section. Figure 1 shows a flow-chart of how the study population was found.

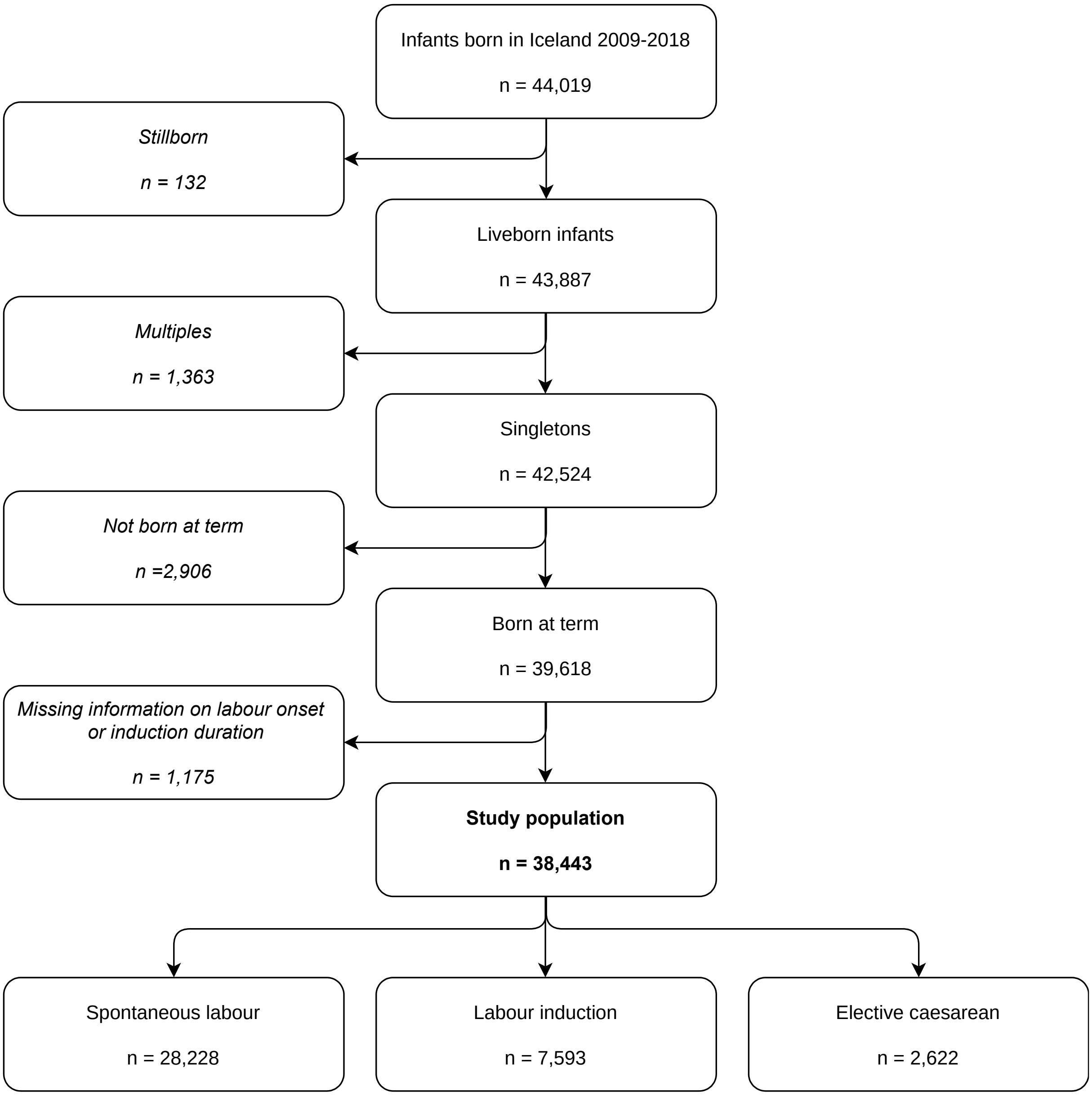


**Figure 1.** Flow-chart showing the study population.

## 3.2 Variables

All variables were obtained from the Icelandic Medical Birth Register. Explanatory variables included labour onset type, labour induction duration and reason for labour induction. The outcome variable was infants' need for monitoring after birth.

### 3.2.1 Explanatory variables

For the first aim of this study, to examine infants need for monitoring after birth based on labour onset, the variable labour onset was used. The variable had four possible values “spontaneous labour”, “labour induction”, “elective caesarean” and “missing”. Infants in the missing category were excluded from the study.

In the Medical Birth Registry, labour induction duration was expressed as number of minutes from beginning of induction of labour until birth. The variable was made categorical, and the women divided into three group based on labour induction duration: “<12 hours”, “12 - 48 hours” and “>48 hours”. Those who had minus values or a labour induction time over 6,000 minutes were excluded from the study, as it was believed to be an unrealistic induction duration. The grouping was made based on results from Blackwell et al. (41) for labour induction duration, where 69.3% of women had delivered within 24 hours, and only 5.7% remained undelivered after 48 hours of labour induction. In this study, women who delivered their baby <12 hours after start of labour induction were categorized as having a short labour induction duration, 12 – 48 hours as having a normal induction duration, and >48 hours as having a long labour induction duration.

The variable “mother’s first 15 diagnosis” was used to identify the reason for labour induction. The variable uses the ICD-10 classification system to indicate conditions associated with the pregnancy or the delivery. Women undergoing labour induction were grouped based on ICD-10 codes according to the most common and severe indications for labour induction, based on the unpublished results from Swift et al., where an expert panel consisting of obstetricians and midwives identified common indications for induction of labour in Iceland. Table 1 shows the ICD-10 codes and code descriptions for labour induction indications. The indications are ranked according to severity. If a woman had more than one indication, she was categorized in the group with the highest ranking, as a higher ranking indicates a more severe induction indication. Groups 6 – 9 were combined into one category as “other medical reasons” for labour induction. Groups 10 and 11 include women who had their labour induced based on gestational or maternal age, when none of the ICD-10 codes in the groups above were registered. Those who had their labour induced but did not have any of the ICD-10 codes from table 1 and did not have their labour induced based on gestational age >41 weeks or maternal age >40 years, were categorised into the “other” group. This group is also referred to as elective induction in the study.

**Table 1.** ICD-codes and descriptions for indications for labour induction, ranked based on severity.

| | ICD-10 codes | Code description |
|---|---|---|
| **1** | **Pre-eclampsia and eclampsia in pregnancy** | |
| | O14<br>O15.0<br>O11 | Pre-eclampsia in pregnancy<br>Eclampsia in pregnancy<br>Pre-eclampsia superimposed on chronic hypertension |
| **2** | **Pregestational diabetes** | |
| | O24.0 O24.1, O24.3 | Pre-existing diabetes mellitus |
| **3** | **Suspected placental insufficiency** | |
| | O36.3<br>Z35.2<br><br>O36.5<br>O41.0 | Maternal care for signs of foetal hypoxia<br>Supervision of pregnancy with other poor reproductive and obstetric history<br>Maternal care for poor foetal growth (IUGR)<br>Oligohydramnios |
| **4** | **Hypertensive disorders (other than preeclampsia)** | |
| | O10.0 and I10<br><br>O13<br>O16 | Pre-existing essential hypertension complicating pregnancy, childbirth and the puerperium<br>Gestational hypertension<br>Unspecified maternal hypertension |
| **5** | **Gestational diabetes** | |
| | O24.4 and O24.9 | Gestational diabetes mellitus |
| **6** | **Obstetric cholestasis** | |
| | O26.6 | Obstetric cholestasis |
| **7** | **Rhesus isoimmunization** | |
| | O36.0, O36.1 | Maternal care for rhesus isoimmunization |
| **8** | **Maternal wellbeing, other** | |
| | O26.7<br>Z65.9<br>O26.8<br>Z35.8 | Subluxation of symphysis pubis in pregnancy<br>Problem related to unspecified psychosocial circumstances<br>Exhaustion and fatigue<br>Supervision of other high-risk pregnancy |
| **9** | **Foetal wellbeing, other** | |
| | O40<br>O66.2<br>O32.0 | Polyhydramnios<br>Macrosomia<br>Maternal care for unstable lie of foetus |
| **10** | **Gestational age>41 weeks** | |
| **11** | **Maternal age>40 years** | |

### 3.2.2 Outcome variable

The outcome of this study was infant's need for monitoring after birth. Infants were divided into three groups: "routine care", "monitoring labour and delivery ward" and "monitoring in the neonatal intensive care unit". The latter two categories were not combined into one "monitoring" category, as there is a substantial difference between infants in need for monitoring in the maternity ward and those in need for monitoring in the special care ward.

### 3.2.3 Confounding variables

Parity is a possible confounder in the study. Layered analysis was used to evaluate the effects of parity on infants' risk for monitoring. Infants were divided into two categories based on their mother's parity;

"primipara" if the mother was giving birth for the first time, and "multipara" for any subsequent births by the mother.

### 3.2.4 Other variables

A few variables were used solely to get an overview of the study population.

Year of birth was divided in two groups, infants born 2009-2013 and infants born in 2014-2018. Gestational age was presented as weeks based on ultrasound. Mothers age at birth was treated as a continuous variable and mothers were categorized as "Icelandic" or "other" based on their nationality. Infants' weight at birth was treated as a continuous variable.

## 3.3 Statistical analysis

The data from the Icelandic Medical Birth Register was received in Microsoft Excel. All statistical analysis was conducted in R version 3.3.3.

Chi-square tests were used to compare infant monitoring groups, where the null hypothesis of no difference between groups was tested. The alpha level for statistical significance was set at $p \leq 0.05$. First, a comparison of all three labour onset groups was made. Later the "routine care" group was used as reference group and the other two outcome groups compared to that group in order to calculate p-values for two category comparisons.

## 3.4 Ethics

This study was approved by the National Bioethics Committee on the 28th of April 2020 (reference number: VSNb2019020007/03.01).

# 4 Results

## 4.1 Baseline characteristics

A total of 38,443 singleton term-born infants born in Iceland during the years 2009-2018. Table 2 shows the characteristics of the study population at labour onset.

The great majority of infants were born after spontaneous labour, 28,228 infants (73.4%), while 7,593 infants (19.8%) were born after their mothers had their labour induced and 2,622 infants (6.8%) were born after an elective caesarean section. There was an increase in labour induction during the study period, 17.1% of women had their labour induced during the years 2009-2013 compared to 22.7% in 2014-2018.

Labour induction was proportionally most likely to be performed among infants born in gestational week 37 (33.3%), followed by week 41 (28.1%). Proportionally, women in gestational week 40 were the most unlikely to have their labour induced (13.4%). The pattern was different among those undergoing elective caesarean section, where women in gestational week 39 were proportionally most likely to have an elective caesarean section (15.6%), but proportionally the fewest elective caesareans were performed in gestational weeks 40 (1.5%) and 41 (0.9%).

Mothers mean age when giving birth was 30.5 (SD 5.41) years, and women who had an elective caesarean section were the oldest labour onset group, with a mean age of 33.4 (SD 5.30) years. A higher percentage of Icelandic women (20.3%) had their labour induced in comparison to women of other nationalities (15.9%). There were more primipara mothers (21.5%) among women undergoing labour induction than multipara mothers (18.6%). Infants mean weight at birth across all labour onset groups was 3,690 g (SD 477). Infants born after labour induction had the same mean weight with a slightly higher standard deviation, 3,690 g (SD 539) compared to the total population.

**Table 2.** Characteristics of mothers and singleton, term-born infants born in Iceland 2009-2018 (n= 38443).

| | **Spontaneous labour** (n=28228) | **Labour induction** (n=7593) | **Elective caesarean** (n=2622) | **Total** (n=38443) |
|---|---|---|---|---|
| **Year of birth** | | | | |
| 2009-2013 | 15365 (76.4%) | 3434 (17.1%) | 1322 (6.6%) | 20121 (100.0%) |
| 2014-2018 | 12863 (70.2%) | 4159 (22.7%) | 1300 (7.1%) | 18322 (100.0%) |
| **Gestational age**[1] | | | | |
| 37 weeks | 1001 (56.6%) | 590 (33.3%) | 178 (10.1%) | 1769 (100.0%) |
| 38 weeks | 2822 (62.8%) | 1140 (25.4%) | 529 (11.8%) | 4491 (100.0%) |
| 39 weeks | 7263 (68.5%) | 1684 (15.9%) | 1648 (15.6%) | 10595 (100.0%) |
| 40 weeks | 10951 (85.1%) | 1728 (13.4%) | 190 (1.5%) | 12869 (100.0%) |
| 41 weeks | 6191 (71.0%) | 2451 (28.1%) | 77 (0.9%) | 8719 (100.0%) |
| **Mother's age at birth** | | | | |
| Mean (SD) | 30.1 (5.22) | 31.1 (5.76) | 33.4 (5.30) | 30.5 (5.41) |
| **Mother's nationality** | | | | |
| Icelandic | 24377 (72.6%) | 6807 (20.3%) | 2319 (6.9%) | 33503 (100.0%) |
| Other | 3851 (78.0%) | 786 (15.9%) | 303 (6.1%) | 4940 (100.0%) |
| **Parity** | | | | |
| Primipara | 11522 (75.5%) | 3279 (21.5%) | 468 (3.1%) | 15269 (100.0%) |
| Multipara | 16706 (72.1%) | 4314 (18.6%) | 2154 (9.3%) | 23174 (100.0%) |
| **Weight at birth**[2] | | | | |
| Mean (SD) | 3690 (455) | 3690 (539) | 3670 (507) | 3690 (477) |

[1]Gestational age in weeks based on ultrasound.

[2]Weight presented in grams.

## 4.2 Infants' need for monitoring after birth based on labour onset

Table 3 shows infants' rate for needing monitoring based on labour onset. The rate for infants only requiring routine care after birth was highest among infants born after an elective caesarean, 93.8%, in comparison to 91.1% and 91.7% among spontaneous labour onset and labour induction, respectively. The highest rate (4.3%) for infant monitoring in the labour and delivery ward was among infants born after spontaneous labour. This group had however the lowest monitoring rate in the NICU (4.6%). The highest NICU rate was among infants born after labour induction (7.3%).

All chi-square tests were statistically significant, allowing rejection of the null hypothesis of no difference in infant monitoring rates between labour onset groups.

**Table 3**. Relationship between labour onset type and singleton term-born infants need for monitoring after birth in Iceland 2009-2018 (n=38443).

| | Spontaneous labour (n = 28228) | Labour induction (n = 7593) | Elective caesarean (n = 2622) | p-value |
|---|---|---|---|---|
| **Infant monitoring n (%)** | | | | <0.001[1] |
| **Routine care** | 25716 (91.1) | 6966 (91.7) | 2460 (93.8) | |
| **Monitoring in the labour and delivery ward** | 1226 (4.3) | 72 (0.9) | 26 (1.0) | <0.001[2] |
| **Monitoring in the neonatal intensive care unit** | 1286 (4.6) | 555 (7.3) | 136 (5.2) | <0.001[3] |

[1] Chi-square test – comparison of all categories in infant monitoring.

[2] Chi-square test – infant routine care vs. monitoring in the labour and delivery ward.

[3] Chi-square test – infant routine care vs. monitoring in the neonatal intensive care unit.

## 4.3 Infants' need for monitoring after birth based on labour onset by parity

Table 4 shows infants' rates for monitoring after birth based on labour onset after stratifying by parity. Of 15,269 primipara mothers, 4,314 had their labour induced (28.3%), whereas there were 3,279 labour induction performed among 23,174 multipara mothers (14.1%). Labour induction was therefore more frequent among primipara mothers during the study period. The frequency of elective caesarean sections was however higher among multipara mothers (9.3%) than primipara mothers (3.1%).

Looking at the spontaneous labour onset group, there was a higher percentage of infants born to primipara mothers than multipara mothers in need of monitoring in the NICU after birth (6.6% vs. 3.1%). On the contrary, there was a higher rate of infant monitoring in the labour and delivery ward among infants born to multipara mothers than primipara mothers (4.9% vs. 3.5%).

Among infants born after labour induction, infants born to primipara mothers had a higher percentage of infants monitored in the NICU compared to infants born to multipara mothers (9.9% vs. 5.4%). Infants born to primipara mothers who had their labour induce had the highest NICU monitoring rate of all labour onset groups, both among primipara and multipara mothers. A similar percentage of infants were monitored in the labour and delivery ward between primiparas (1.0%) and multiparas (0.9).

Chi-square test comparing all three categories of infant monitoring was statistically significant. This was also the case for chi-square tests comparing infants monitored in the labour and delivery ward or in the NICU compared to infants routinely cared for.

**Table 4**. Relationship between labour onset type and singleton term-born infants need for monitoring after birth, stratified by parity (n=38443).

| | | Spontaneous labour (n = 28228) | Labour induction (n = 7593) | Elective caesarean (n = 2622) | p-value |
|---|---|---|---|---|---|
| **Primipara mothers** (n=15269) | **Infant monitoring n (%)** | | | | <0.001[1] |
| | Routine care | 10351 (89.8%) | 2922 (89.1%) | 438 (93.6%) | |
| | Monitoring in the labour and delivery ward | 408 (3.5%) | 34 (1.0%) | 3 (0.6%) | <0.001[2] |
| | Monitoring in the neonatal intensive care unit | 763 (6.6%) | 323 (9.9%) | 27 (5.8%) | <0.001[3] |
| **Multipara mothers** (n=23174) | **Infant monitoring n (%)** | | | | <0.001[1] |
| | Routine care | 15365 (92.0%) | 4044 (93.7%) | 2022 (93.9%) | |
| | Monitoring in the labour and delivery ward | 818 (4.9%) | 38 (0.9%) | 23 (1.1%) | <0.001[2] |
| | Monitoring in the neonatal intensive care unit | 523 (3.1%) | 232 (5.4%) | 109 (5.1%) | <0.001[3] |

[1] Chi-square test – comparison of all categories in infant monitoring.

[2] Chi-square test – infant routine care vs. monitoring in the labour and delivery ward.

[3] Chi-square test – infant routine care vs. monitoring in the neonatal intensive care unit.

## 4.4 Infants rates for monitoring after birth based on labour induction duration

Infants born after a short induction duration had the highest rate (93.5%) for only needing routine care after birth of the three labour induction duration groups (Table 5). This group was also the one with the lowest proportion of infants admitted to the NICU (5.7%) of the three labour onset groups. The highest rate for monitoring in the NICU was among infants born after a normal labour induction duration, lasting between 12-48 hours (8.6%). Infants born after a long labour induction duration, lasting 48 hours or more, had a NICU admission rate of 8.0%, but notice must be made of how small the group is. The monitoring rate in the maternity ward was similar for all three labour onset groups.

There was a statistically significant difference between groups when comparing all three monitoring groups as well as when infants not in need for monitoring and infants monitored in the NICU were compared. Chi-squared test did not show a statistically significant difference when infants not in need for monitoring were compared to infants in need for monitoring in the maternity ward, which may be due to the small number of infants in the group with a long labour induction duration needing monitoring in the labour and delivery ward (n = 2).

**Table 5**. Relationship between labour induction duration (hours) and infants need for monitoring after birth, only infants born after induced labour (n=7593).

| | **Short induction duration, ≤ 12h (n = 3272)** | **Normal induction duration, 12h-48h (n = 4071)** | **Long induction duration, ≥ 48h (n = 250)** | **p-value** |
|---|---|---|---|---|
| **Infant monitoring n (%)** | | | | <0.001[1] |
| **Routine care** | 3058 (93.5) | 3680 (90.4) | 228 (91.2) | |
| **Monitoring in the labour and delivery ward** | 29 (0.9) | 41 (1.0) | 2 (0.9) | 0.781[2] |
| **Monitoring in the neonatal intensive care unit** | 185 (5.7) | 350 (8.6) | 20 (8.0) | <0.001[3] |

[1] Chi-square test – comparison of all categories in infant monitoring.

[2] Chi-square test – infant routine care vs. monitoring in the labour and delivery ward.

[3] Chi-square test – infant routine care vs. monitoring in the neonatal intensive care unit.

## 4.5 Infants rates for monitoring after birth based on labour induction indication

When monitoring rates among infants born after labour induction were observed in relation to the indication for labour induction, the group of infants whose mothers had pre-gestational diabetes stands out with the lowest rate of infants only needing routine care (76.8%) and the highest rate for monitoring in the NICU (22.0%) (Table 6). Infants born to mothers diagnosed with gestational diabetes had a proportion of 6.3% of infants monitored in the NICU. The most common reason for labour induction was gestational age > 41 weeks (22.5%).

Infants in the “other” group are born to mothers who had their labour induced but did not have any of the ICD-10 codes listed in table 1 registered in the Icelandic Medical Birth Registry. These induction are therefore classified as elective labour induction in this study and make up of 19.6% of all labour induction during the study period. Infants rate for NICU admissions in this group was 6.7%, whereas 1.4% needed monitoring in the labour and delivery ward.

Chi-square test comparing all categories in infant monitoring was statistically significant, indicating that there is a difference between the reason for labour induction and the degree of monitoring needed after birth. This was also true for the chi-test comparing routine care and monitoring in the NICU, but the null hypothesis of no difference between groups cannot be rejected when comparing the groups of infants’ routine care vs. monitoring in the labour and delivery ward. Again, this analysis is conducted on a very small number of infants needing monitoring in the labour and delivery ward, which may be a possible explanation for the high p-value.

**Table 6**. Relationship between infants need for monitoring after birth and the reason for labour induction, only infants born after induced labour (n=7593).

| | **Pre-eclampsia and eclampsia in pregnancy (n = 774)** | **Pregesta-tional diabetes (n = 82)** | **Suspected placental insufficiency (n=596)** | **Hypertensive disorders (other than pre-eclampsia) (n = 867)** | **Gestational diabetes (n =1002)** | **Other medical reasons[1] (n = 927)** | **Gestational age >41 weeks (n=1710)** | **Maternal age>40 years (n=145)** | **Other (n = 1490)** | **p-value** |
|---|---|---|---|---|---|---|---|---|---|---|
| **Infant monitoring n (%)** | | | | | | | | | | <0.001[2] |
| **Routine care** | 690 (89.1) | 63 (76.8) | 540 (90.6) | 791 (91.2) | 928 (92.6) | 855 (92.2) | 1587 (92.8) | 136 (93.8) | 1376 (92.3) | |
| **Labour and delivery ward** | 8 (1.0) | 1 (1.2) | 3 (0.5) | 11 (1.3) | 11 (1.1) | 6 (0.7) | 16 (0.9) | 2 (1.4) | 14 (0.9) | 0.874[3] |
| **Neonatal intensive care unit** | 76 (9.8) | 18 (22.0) | 53 (8.9) | 65 (7.5) | 63 (6.3) | 66 (7.1) | 107 (6.3) | 7 (4.8) | 100 (6.7) | <0.001[4] |

[1] Other medical reasons include obstetric cholestasis, rhesus isoimmunization, maternal wellbeing (subluxation of symphysis pubis in pregnancy, problem related to unspecified psychosocial circumstances, exhaustion and fatigue, supervision of other high risk pregnancy) and foetal wellbeing (polyhydramnios, macrosomia and maternal care for unstable lie of foetus).

[2] Chi-square test – comparison of all categories in infant monitoring.

[3] Chi-square test – infant routine care vs. monitoring in the labour and delivery ward.

[4] Chi-square test – infant routine care vs. monitoring in the neonatal intensive care unit.

# 5 Discussion

## 5.1 Main findings

This retrospective cohort study studied rates of infant monitoring after birth according to labour onset and duration of induction of labour during 2008-2018 in Iceland. Of the three labour onset groups, infants born after labour induction had the highest rate of monitoring in the NICU (7.3%), while infants born after a spontaneous labour had the lowest NICU monitoring rate (4.6%). Infants born after an elective caesarean had the highest rate for only needing routine care of the three labour onset groups. Statistical analysis of the data showed that labour onset type does have a significant effect on infants need for monitoring after birth. A higher rate of labour induction was seen among primipara mothers compared to multipara mothers. The NICU admission rate after labour induction was also higher among infants born to primiparas compared to multiparas (9.9% vs. 5.4%).

The majority of labour induction during the study period had a normal induction duration, lasting between 12 – 48 hours (53.6%). Only 250 (3.3%) of 7,593 performed labour induction were classified as long induction duration, lasting 48 hours or longer. The highest rate of monitoring in the NICU (8.6%) was seen among infants born after a normal labour induction duration, lasting from 12 – 48 hours. The lowest NICU monitoring rate was among infants born after short labour induction duration of 12 hours or less (5.7%).

The group of infants born to mothers with pre-gestational diabetes stood out with the highest rate of monitoring in the NICU (22.0%), which is noticeably higher than any other category. In analysing data from this study population, 19.6% of labour induction are categorised as being elective as they did not have a medical indication for induction. This was the second most common reason for labour induction, exceeded only by gestational age exceeding 41 weeks. Of infants born after an elective labour induction, 6.7% were admitted to the NICU for monitoring. This rate is similar to other indications that can be categorized as soft indications, like gestational and maternal age, as they are not indicators for underlying medical conditions. The more definite indications like pre-eclampsia/eclampsia and presentational diabetes resulted on the other hand in higher NICU monitoring rates.

### 5.1.1 Labour induction in Iceland

This study found the highest need for NICU monitoring to be among infants born after labour induction. This trend of higher monitoring need among infants after labour induction has also been noted in studies comparing odds for NICU admission based on whether infants are born after labour induction or spontaneous labour (83, 84). Contrasting these results with findings from abroad can be difficult, as registration protocols and the base of analysis for studies vary across countries. Neonatal outcomes from an Austrian population study (83) did in many ways resemble our study, both being population-based studies, starting in 2008, although our study analysed data over a longer timespan (10 years vs 5 years). The labour induction rate was practically the same in both studies, 19.7% in the Austrian study vs. 19.8% in our study. The Austrian study did not include planned caesarean sections in its analysis, but the authors did control for potential confounders. The study did find increased odds of NICU admission after labour induction compared to spontaneous labour after controlling for gestational age, mother's age, BMI, parity, duration of labour, birth weight, mode of delivery and year of birth (83). Braud et al. (2013) studied neonatal outcomes after elective labour induction and medically indicated labour induction (84). They did nevertheless include data from a spontaneous labour group to allow for comparison with other studies. The study conducted a separate analysis based on parity. The odds for NICU admission after labour induction compared to spontaneous labour were OR 1.51 (95%CI 1.15; 1.90) among multiparas, but the among primiparas was the OR 1.39 (95%CI 1.15; 1.69). Our study found a higher admission rate among infants born to primipara mothers. Possible explanations for the difference may be that our study stratified by parity, while Braud et al. (2013) did separate analyses. The confidence intervals in Braud's et al. (2013) study were wide, indicating a need for further studies in the field.

Studies that have compared the difference in NICU admissions based on labour induction versus expectant management have found a lower risk for NICU admissions for infants born after labour induction (53, 54). It has been argued that comparing labour induction to spontaneous labour can lead to exaggerated estimates of risks. Comparing labour induction to expectant management, where the pregnancy is continued until the onset of labour and a prospective approach is taken, is believed to be a more relevant comparison, especially if their results are to be used in clinical practice. This is due to the fact that the decision to induce labour can be taken at any time, but it is not possible to determine when a spontaneous labour will start. When expectant management is the category of comparison, a decision on whether labour induction would be beneficial is taken at that timepoint, rather than not inducing labour. Comparing labour induction to spontaneous labour does however give an overview of patterns, in this case of the magnitude of infant monitoring needed (94). This may be the reason for the differences in results found in the Teitler et al. (2019) paper and the ARRIVE trial, as one study employs a retrospective approach while the other uses a prospective approach (11, 85).

Dunne et al. (2009) did not find statistical differences in NICU admission among infants born after spontaneous labour, elective labour induction or elective caesarean sections (59), while Teitler et al. (2019) found a higher risk for NICU admissions among infants born after labour induction (85). Both studies excluded all women with any medical or surgical complications of pregnancy, which makes comparison to our study complicated (59, 85).

Present study found that infants born after elective caesarean had the highest rate of infants only requiring routine care following birth, nevertheless, this group had a higher NICU monitoring rate than the spontaneous labour group. This is consistent with other studies comparing NICU admission rates based on elective caesarean sections or spontaneous labour, where no association has been found and lower risks for NICU admissions following planned caesarean (73, 74). These studies did however only include primipara mothers while this study also included multipara mothers. The fact that the elective caesarean group had a higher rate of routine care only highlights the importance of taking all monitoring aspects into consideration, to get a holistic overview of infants monitoring needs. This has also been pointed out by Braun et al. (2020) (76). It is interesting to see that the monitoring rate in the labour and delivery ward is highest among infants born after spontaneous labour, which is also the group with the lowest monitoring rate in the NICU. This indicates that the monitoring need is not as urgent for infants born after spontaneous labour compared to those born after labour induction.

The fact that infants born after labour induction have the highest NICU monitoring rate of the three labour onset groups highlights the necessity of studying the effects of labour induction in Iceland in even greater detail. Labour induction most commonly performed because of a situation where waiting for spontaneous labour can cause harm to the mother or to the infant, which is in line with the WHO's recommendations (3). Further studies that control for labour induction indications and induction methods are needed to be able to conclude whether the high NICU rate is caused by the labour induction or if it is caused by the induction indication, or the labour induction method. This study cannot conclude this relationship as it uses descriptive statistics.

### 5.1.2 Duration of labour induction

A statistically significant difference was observed between labour induction duration groups and monitoring rates for infants. Blackwell et al. (2008) did however, opposite to our study, not find a connection between labour induction duration and NICU admissions (41). The difference between the two studies may be due to a number of reasons. The study by Blackwell et al. (2008) did only include primipara mothers, while our study included both primipara and multipara mothers. There is also a great racial difference between the studies, where 85% of mothers in the Blackwell et al. (2008) study were African American, but in our study 89.6% of mothers had Icelandic nationality, so it is likely that most of the women are of white race. Other differences between the studies that may explain the different results are the study duration and number of participants, but our study has a much larger study population. There was also a difference in grouping, as the Blackwell et al. (2008) study used a different classification scheme; <24 hours, 24-48 hours and >48 hours. For this study the first two categories were split differently: 12 hours or shorter, 12-48 hours and 48 hours or longer. This distinction was made to fit the Icelandic data better. Both studies did however examine the total duration from start of labour induction until delivery, which has not been done in many studies. Cheng et al. (2009) found an increased risk for NICU admissions with an increased length of the first stage of labour. Like present study, Cheng et al. (2009) included both primipara mothers as well as multipara mothers (42). The study population also resembled the present study regarding race compared to Blackwell et al. (2008), as 42% of the study population was white. However, Cheng et al. (2009) looked at the first stage of labour, and not the duration from labour induction to delivery, like our study and Blackwell et al. (2008) study did (41, 42).

Studying the whole duration from start of labour induction to delivery is not a common approach. Most studies look at a specific stage or phase of labour or use other conditions more specific on the study areas, such as labour induction methods or labour induction indications. The fact that this study has shown that there is a difference in monitoring rates based on labour induction duration highlights the importance of studying the topic even further in order to out more precisely identify where the difference lies. This study could not explore if, and at what stage of labour there was a difference between spontaneous labour and labour induction. Previous studies have found that the difference in duration is in the latent phase, where women undergoing labour induction have a longer median labour time. It would also be interesting for future studies to view the induction duration based on labour induction indications, as studies have shown that there may be differences in both hospital stay and labour duration based on whether the induction was decided on due to medical or elective reasons (15, 38). It is also interesting to see if race affects the association, which might be contributing to the difference in the present study results to the Blackwell et al (41). Stratifying by parity may also have been an advantage when looking at the labour induction duration, as primipara mothers have shown to have a longer average labour duration than multipara mothers (14).

Based on this, it is evident that more research is needed on the effects of labour induction duration and infant monitoring, as studies show conflicting results.

### 5.1.3 Labour induction indications

In the present study, the most common labour induction indication was gestational age exceeding 41 weeks. A number of previous studies have found better neonatal outcomes, including lower mortality and NICU admissions if labour is induced somewhere in gestational week 41, compared to expectant management (52-54), while there are others that do not recommend labour induction prior to post-term (55). An Icelandic study by Karlsdóttir et al. (2019), highlights the importance of weighing the benefits and risks associated both with labour induction and with a continued pregnancy when deciding if and when labour should be induced (56).

The second most common reason for labour induction was elective induction and the third most common reason was gestational diabetes. In March 2012, the most common indications for labour induction at Landspítali were PROM, gestational age (usually performed after gestational week 41+6) and pre-eclampsia/hypertension (66). When comparing these studies, it is important to take into account the small study population in the study by Ragnarsdóttir (66). In our study, PROM was not considered as an labour induction indication, as it can be argued for that labour has already begun when the membranes ruptures. Labour induction indications are changing over time, like the compartment of our study to Ragnarsdóttir (2013) study shows (66). This shift may be due to an increase in risk-related factors over time (5). This is however not necessarily the only reason for the rising induction rate, as a recent study concluded that the largest increase in labour induction was among women without a diagnosis of hypertensive disorders or diabetes (46). This finding is supported by the present study, which found that elective labour induction was among the most common reasons for labour induction.

An alarming 22.0% of infants born to mothers diagnosed with pre-gestational diabetes needed monitoring in the NICU. This was also the induction indication with the highest NICU admission rate among infants in Sydney in 2009-2016 (86). Pre-gestational diabetes has been linked to increased adverse neonatal outcomes (45). It would be interesting to see further studies on how these factors play together and what the actual effect of the labour induction has on NICU admissions among infants born to mothers with pre-gestational diabetes. There has been a substantial increase in diabetes in Iceland over the last years (46). Healthcare professionals are aware of the increase and the risks associated with diabetes during pregnancy, and women with known risk factors are under supervision during their pregnancy and their pregnancy is classified as high-risk. The findings of this study support the need for extensive monitoring of infants born to expectant mothers with pre-gestational diabetes.

It can be problematic to compare elective labour induction rates as there is no standardised definition of elective labour induction and what can be classified as logical reasons can be a rather subjective evaluation. This study categorises labour induction performed on women without any of the ICD-10 codes shown in table 1, as elective labour induction. The ICD-10 codes in the table have been identified as the most common and severe indications for labour induction in Iceland by an expert panel. Based on this, elective labour induction made up 19.6% of all labour induction during the study period. Studies comparing infants risk for NICU admission after elective labour induction versus expectant management are not compatible but do either not find a difference in risk between the groups (11, 62), or find an increased risk (12, 38). The elective induction rate must be taken with some precautions, as previous Icelandic studies have drawn attention to the fact that the registration of indications for labour induction have been deficient and uncoordinated (66). As this category includes every case which cannot be classified in another category, it is difficult to know the exact reason for placing someone in the category.

It is interesting to see that elective labour induction, gestational age > 41 weeks and maternal age > 40 years have similar NICU monitoring rates. These indications are not based on medical conditions but are nevertheless indications for labour induction. A large systematic scoping review by Coates et al. (2019) on clinical indications for labour induction finds strong evidence for labour induction for post-term pregnancies, but states that further research on the effect on maternal age is required (44). In our study, the more definite indications for induction of labour, like pre-gestational diabetes and pre-eclampsia do show a higher NICU monitoring rate. These indications are definite risk factors for the infants growth and development after birth. According to Coates et al. (2019) better quality evidence is needed on labour induction and diabetes as well as quality evidence on when to perform labour induction for women with pre-eclampsia (44).

It is vital to have high-quality information on the effects of elective labour induction, as healthcare personnel must be able to educate expectant mothers on possible risks so that they can take an informed decision. This is especially important in the light of recent changes, where labour induction are beginning to be viewed as a reasonable option for low-risk primipara pregnancies.

## 5.2 Strengths and limitations

This study's main strength was that it used data from the Icelandic Medical Birth Registry, including information on all births in Iceland during the study period. This strengthens the generalisability of the study, as access to population data is not always available to researchers. This is also a necessity in the light of the rather small numbers of infants in need for monitoring each year, which limits the statistical power of the analysis of small subgroups. Another strength was the length of the study period, from 2009-2018. As the total number of births per year is not especially high in Iceland, there is risk for fluctuations in statistics if the study period is short. An even longer study period would not necessarily be an advantage for this study, as protocols and induction methods in Iceland have been changing over the years. One example of such changes were the rules of procedure at Landspítali changed from the use of dinoprostone to Misoprostol in 2008 (66), so having a longer study period may make it more difficult to generalise and potentially affected the reliability of the study. Another strength of the study is that infants were classified by the severity of monitoring need. This gives a better understanding of the scale of the problem, as Braun et al. (2020) points out (76).

Among the limitations of the study is the possibility of misclassification, as 1.116 infants belonging to the labour induction group were excluded from the analysis based on missing data on labour induction duration. This exclusion is unlikely to have had an effect on the analysis, as the misclassification was most likely random and not related to infant monitoring. Another limitation is the possible misclassification of infants into groups of induction indications. It can for example be difficult to distinguish between preeclampsia/eclampsia and other hypertensive disorders. Like previously mentioned, there is also risk for misclassification to the elective labour induction group, if registration of indications is not sufficient. Again, this is an effect that can reasonably be assumed to be random, as misclassification is unlikely to be a systematic problem in a dataset as large as the one used in this study. The fact that the precise indication for labour induction is not registered in the Icelandic Medical Birth Registry but a system of classifying women into labour induction indications based on the most common and severe indications, can also cause more rare indications to be classified into the elective induction group. This highlights the importance of better registration and coordination of indications for induction in Iceland, which has been called for in previous studies as well (66). Our study made use of descriptive statistics, but using inferential statistics, such as regression analysis, would enable controlling for potential confounders, like birth weight, gender and factors related to the mother such as age, BMI and social status. Other studies have found that less advantaged women are more likely to have their labour induced (7), and contrasting those results with the Icelandic situation would be worthwhile. Controlling for labour induction indication and induction method would be interesting to see, as this study cannot tell whether the monitoring rates are based on the labour induction indication, the labour induction method or a result of the labour induction itself.

# 6 Conclusion

This study has shed light on the scope of labour induction and infants monitoring needs in Iceland over a ten-year period. Infants born after labour induction require more monitoring and more NICU monitoring, than infants born after spontaneous labour and elective caesarean section. This is especially evident among infants born to primipara mothers. Labour induction duration does also have a significant effect on infants monitoring rates. Healthcare professionals should be aware of this trend as this can affect the load on the NICU. The focus on increasing the rate of infant monitoring in the labour and delivery ward opposed to monitoring in the NICU if possible, is greatly beneficial for the development of the infant and the overall health of the family. Elective labour induction is beginning to be accepted as a reasonable option among certain groups, but this study has highlighted the risk of undesirable infant outcomes should that be the case. Therefore, further studies on this matter are urgent, especially as elective labour induction is among the most common reason for labour induction in Iceland. Further studies are needed in order to find out if the high NICU rate is caused by the underlying indication for induction or the labour induction itself.

There are many other aspects to labour induction yet to be studied in Iceland, some of them have been named above, but other factors such as maternal outcomes would be beneficial for Icelandic healthcare personnel as well as expecting parents to be aware of. Research in the field of labour induction should always be up to date, as this is a rapidly changing field, both in relation to labour induction methods, and known risk factors.

# References


1. World Health Organization (WHO). *Managing Complications in Pregnancy and Childbirth; A Guide for Midwives and Doctors - 2nd ed.* 2017. Available from: https://apps.who.int/iris/bitstream/handle/10665/255760/9789241565493-eng.pdf?sequence=1 [Accessed 20th November 2020].

2. Marconi AM. Recent advances in the induction of labor. *F1000Research*. 2019;8.

3. World Health Organization (WHO). *WHO recommendations for Induction of labour.* 2011. Available from: http://apps.who.int/iris/bitstream/handle/10665/44531/9789241501156_eng.pdf?sequence=1 [Accessed 26th November 2020].

4. Simpson KR. Cervical Ripening and Labor Induction and Augmentation, 5th Edition. *Nurs Womens Health*. 2020;24(4):1-41.

5. Jónasdóttir E (ed.), Eiríksdóttir VH (ed.). S*kýrsla fæðingarskráningar starfsárið 2018.* Embætti landlæknis, Landspítali. 2020.

6. Colmorn LB, Petersen KB, Jakobsson M, Lindqvist PG, Klungsoyr K, Kallen K, et al. The Nordic Obstetric Surveillance Study: A Study of Complete Uterine Rupture, Abnormally Invasive Placenta, Peripartum Hysterectomy, and Severe Blood Loss at Delivery. *Acta obstetricia et gynecologica Scandinavica*. 2015;94(7):734-44.

7. Carter S, Channon A, Berrington A. Socioeconomic risk factors for labour induction in the United Kingdom. *BMC Pregnancy Childbirth*. 2020;20(1):146.

8. Lindgren CEH. Induced Labour in Sweden, 1992-2012: A Population-Based Cohort Study. *Birth*. 2016;43(2).

9. Ananth CV, Wilcox AJ, Gyamfi-Bannerman C. Obstetrical interventions for term first deliveries in the US. *Paediatr Perinat Epidemiol*. 2013;27(5):442-51.

10. Levine LD, Hirshberg A, Srinivas SK. Term induction of labour and risk of cesarean delivery by parity. *J Matern Fetal Neonatal Med*. 2014;27(12).

11. Grobman WA, Rice MM, Reddy UM, Tita ATN, Silver RM, Mallett G, et al. Labor Induction versus Expectant Management in Low-Risk Nulliparous Women. *The New England journal of medicine.* 2018;379(6):513-23.

12. Grobman WA, Caughey AB. Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies. *American journal of obstetrics and gynecology*. 2019;221(4):304-10.

13. Stock SJ, Ferguson E, Duffy A, Ford I, Chalmers J, Norman JE. Outcomes of elective induction of labour compared with expectant management: population based study. *BMJ*. 2012.

14. Harper LM, Caughey AB, Odibo AO, Roehl KA, Zhao Q, Cahill AG. Normal progress of induced labor. *Obstetrics and gynecology*. 2012;119(6):1113-8.

15. Dögl M, Romundstad P, Berntzen LD, Fremgaarden OC, Kirial K, Kjollesdal AM, et al. Elective induction of labor: A prospective observational study. *PLoS One*. 2018;13(11).

16. Kenny LC (ed.), Myers JE (ed.). *Obstetrics*. 20th ed. Boca Raton, FL: Taylor & Francis Group; 2017.

17. Nabi HA, Aflaifel NB, Weeks AD. A hundred years of induction of labour methods. *Eur J Obstet Gynecol Reprod Biol*. 2014;179:236-9.

18. Tenore JL. Methods for Cervical Ripening and Induction of Labour. *American Family Physician*. 2003;67(10).

19. Ezebialu IU, Eke AC, Eleje GU, Nwachukwu CE. Methods for assessing pre-induction cervical ripening. *Cochrane Database Syst Rev*. 2015(6).

20. Greenberg V, Khalifeh A. Intracervical Foley balloon catheter for cervical ripening and labor induction: A review. *Seminars in perinatology*. 2015;39(6):441-3.

21. Wormer KC, Bauer A, Williford AE. *Bishop Score*. StatPearls. Treasure Island, FL: StatPearls Publishing. 2020.

22. Boulvain M, Kelly A, Irion O. Intracervical prostaglandins for induction of labour. *Cochrane Database Syst Rev*. 2008(1).

23. Luckas M, Bricker L. Intravenous prostaglandin for induction of labour. *Cochrane Database Syst Rev*. 2000(4).

24. Sayed Ahmed WA, Ibrahim ZM, Ashor OE, Mohamed ML, Ahmed MR, Elshahat AM. Use of the Foley catheter versus a double balloon cervical ripening catheter in pre-induction cervical ripening in postdate primigravidae. *The journal of obstetrics and gynaecology research*. 2016;42(11):1489-94.

25. Levine LD. Cervical ripening: Why we do what we do. *Seminars in perinatology*. 2020;44(2).

26. Manly E, Hiersch L, Moloney A, Berndl A, Mei-Dan E, Zaltz A et al. Comparing Foley Catheter to prostaglandins for Cervical Ripening in Multiparous Women. *Journal of Obstetrics and Gynaecology Canada.* 2019; 42(7).

27. Girault A, Goffinet F, Le Ray C. Reducing neonatal morbidity by discontinuing oxytocin during the active phase of first stage of labor: a multicenter randomized controlled trial STOPOXY. *BMC Pregnancy Childbirth.* 2020;20(1).

28. Alfirevic Z, Kelly AJ, Dowswell T. Intravenous oxytocin alone for cervical ripening and induction of labour. *Cochrane Database Syst Rev*. 2009(4).

29. Boie S, Glavind J, Uldbjerg N, Bakker JJH, van der Post JAM, Steer PJ, et al. CONDISOX-continued versus discontinued oxytocin stimulation of induced labour in a double-blind randomised controlled trial. *BMC Pregnancy Childbirth.* 2019;19(1).

30. Chopra S, SenGupta SK, Jain V, Kumar P. Stopping Oxytocin in Active Labor Rather Than Continuing it until Delivery: A Viable Option for the Induction of Labor. *Oman Med J*. 2015;30(5):320-5.

31. Finucane EM, Murphy DJ, Biesty LM, Gyte GM, Cotter AM, Ryan EM, et al. Membrane sweeping for induction of labour. *Cochrane Database Syst Rev*. 2020.

32. Smyth RM. Amniotomy for Shortening Spontaneous Labour. *Cochrane Database of Systematic Reviews*. 2013.

33. Sheibani L, Wing DA. A safety review of medications used for labour induction. *Expert Opin Drug Saf.* 2018;17(2):161-7.

34. Abalos E, Oladapo OT, Chamillard M, Diaz V, Pasquale J, Bonet M, et al. Duration of spontaneous labour in 'low-risk' women with 'normal' perinatal outcomes: A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2018;223:123-32.

35. Hanley GE, Munro S, Greyson D, Gross MM, Hundley V, Spiby H, et al. Diagnosing onset of labor: a systematic review of definitions in the research literature. *BMC Pregnancy Childbirth*. 2016;16:71.

36. Rhoades JS, Cahill AG. Defining and Managing Normal and Abnormal First Stage of Labor. *Obstet Gynecol Clin North Am*. 2017;44(4):535-45.

37. Schoen C, Navathe R. Failed induction of labor. *Seminars in perinatology*. 2015;39(6):483-7.

38. Souter V, Painter I, Sitcov K, Caughey AB. Maternal and newborn outcomes with elective induction of labor at term. *American journal of obstetrics and gynecology.* 2019;220(3).

39. Jung A, Beckmann M. Predicting the duration of induction of labour in nulliparous women. *Journal of obstetrics and gynaecology*. 2020;40(2):167-70.

40. Rane SM, Guirgis RR, Higgins B, Nicolaides KH. Models for the prediction of successful induction of labor based on pre-induction sonographic measurement of cervical length. *J Matern Fetal Neonatal Med*. 2005;17(5):315-22.

41. Blackwell SC, Refuerzo J, Chadha R, Samson J. Duration of labor induction in nulliparous women at term: how long is long enough? *American journal of perinatology*. 2008;25(4):205-9.

42. Cheng YW, Delaney SS, Hopkins LM, Caughey AB. The association between the length of first stage of labor, mode of delivery, and perinatal outcomes in women undergoing induction of labor. *American journal of obstetrics and gynecology*. 2009.

43. Wilkerson RG, Ogunbodede AC. Hypertensive Disorders of Pregnancy. Emerg Med Clin North Am. 2019;37(2):301-16.

44. Coates D, Makris A, Catling C, Henry A, Scarf V, Watts N, et al. A systematic scoping review of clinical indications for induction of labour. *PLoS One*. 2020;15(1).

45. Maso G, Piccoli M, Parolin S, Restaino S, Alberico S. Diabetes in pregnancy: timing and mode of delivery. *Curr Diab Rep.* 2014;14(7).

46. Swift EM, Tómasson G, Gottfreðsdóttir H, Einarsdóttir K, Zoega H. Obstetric interventions, trends, and drivers of change: A 20-year population-based study from Iceland. *Birth*. 2018;45(4):368-76.

47. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational Diabetes Mellitus: Mechanisms, Treatment, and Complications. *Trends Endocrinol Metab*. 2018;29(11):743-54.

48. Harðardóttir H, Jóhannesson AJ, Guðmundsdóttir A, Hreiðarsson ÁB, Ársælsdóttir BM, Björnsson H et al. Klínískar leiðbeiningar um skimun, greiningu og meðferð sykursýki á meðgöngu. Landspítali. 2012.

49. Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. *Obstetrics and gynecology*. 2014;124(1):120-33.

50. World Health Organization (WHO). *ICD-10: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*. 2004.Available from: https://www.who.int/classifications/icd/ICD10Volume2_en_2010.pdf [Accessed 17th October 2020].

51. National Collaborating Centre for Women's and Children's Health. Induction of Labour; Clinical Guideline. 2008. Available from: https://www.nice.org.uk/guidance/cg70/evidence/cg70-induction-of-labour-full-guideline2 [Accessed 18th February 2021].

52. Wennerholm UB, Saltvedt S, Wessberg A, Alkmark M, Bergh C, Wendel SB, et al. Induction of labour at 41 weeks versus expectant management and induction of labour at 42 weeks (SWEdish Post-term Induction Study, SWEPIS): multicentre, open label, randomised, superiority trial. *BMJ*. 2019.

53. Middleton P, Shepherd E, Crowther CA. Induction of labour for improving birth outcomes for women at or beyond term. *Cochrane Database Syst Rev*. 2018.

54. Middleton P, Shepherd E, Morris J, Crowther CA, Gomersall JC. Induction of labour at or beyond 37 weeks' gestation. *Cochrane Database Syst Rev*. 2020.

55. Rydahl E, Eriksen L, Juhl M. Effects of induction of labor prior to post-term in low-risk pregnancies: a systematic review. *JBI Database System Rev Implement Rep*. 2019;17(2):170-208.

56. Ólafsdóttir ÁH, Kristófersson DM, Karlsdóttir SI. Áhrif framköllunar fæðinga eftir 41. viku meðgöngu á fæðingarmáta og útkomu fæðinga. *Læknablaðið*. 2019;105(03):115-23.

57. The American College of Obstetricians and Gynecologists (ACOG). ACOG Committee Opinion No. 765: Avoidance of Nonmedically Indicated Early-Term Deliveries and Associated Neonatal Morbidities. *Obstet Gynecol*. 2019.

58. The American College of Obstetricians and Gynecologists (ACOG). ACOG Practice Bulletin No. 107: Induction of labor. *Obstet Gynecol*. 2009.

59. Dunne C, Silva OD, Schmidt G, Natale R. Outcomes of Elective Labour Induction and Elective Caesarean Section in Low-risk Pregnancies Between 37 and 41 Weeks' Gestation. *Journal of Obstetrics and Gynaecology Canada*. 2009;31(12):1124-30.

60. B Coulm BB, S Alexander, M Boulvain, C Le Ray. Elective induction of labour and maternal reques: a national population-based study. *An International Journal of Obstetrics and Gynaecology.* 2015.

61. Gallagher PJ, Liveright E, Mercier RJ. Patients' perspectives regarding induction of labor in the absence of maternal and fetal indications: Are our patients ready for the ARRIVE trial? *Am J Obstet Gynecol MFM.* 2020;2(2):100086.

62. Saccone G, Della Corte L, Maruotti GM, Quist-Nelson J, Raffone A, De Vivo V, et al. Induction of labor at full-term in pregnant women with uncomplicated singleton pregnancy: A systematic review and meta-analysis of randomized trials. *Acta obstetricia et gynecologica Scandinavica*. 2019;98(8):958-66.

63. Keulen JK, Bruinsma A, Kortekaas JC, van Dillen J, Bossuyt PM, Oudijk MA, et al. Induction of labour at 41 weeks versus expectant management until 42 weeks (INDEX): multicentre, randomised non-inferiority trial. *BMJ*. 2019;364:l344.

64. Vernharðsdóttir AS, Gunnarsdóttir EA. Árangursmælar á fæðingarvakt. *Ljósmæðrablaðið*. 2016:18-21.

65. Landspítali. Gæðaskjal: Verklagsregla: 15.01 Framköllun fæðingar - ábendingar. 2018. Available from: https://traveler.lsh.is/focal/gaedahandbaekur/gnhskurda.nsf/0/1FC5AA668C05775300257E7600541856 [Accessed 24th March 2021].

66. Ragnarsdóttir HS. Inngrip í fæðingarferlið. *Journal of the Icelandic Midwives Association*. 2013;2(91):15-8.

67. Devillard E, Delabaere A, Rouzaire M, Pereira B, Accoceberry M, Houlle C, et al. Induction of labour in case of premature rupture of membranes at term with an unfavourable cervix: protocol for a randomised controlled trial comparing double balloon catheter (+oxytocin) and vaginal prostaglandin (RUBAPRO) treatments. *BMJ Open*. 2019;9(6).

68. Boerma T, Ronsmans C, Melesse DY, Barros AJD, Barros FC, Juan L, et al. Global epidemiology of use of and disparities in caesarean sections. *The Lancet.* 2018;392(10155):1341-8.

69. Euro-Peristat Project. European Perinatal Health Report: Core indicators of the health and care of pregnant women and babies in Europe in 2015. 2018. Available from: https://www.europeristat.com/images/EPHR2015_Euro-Peristat.pdf [Accessed 27th March 2021].

70. World Health Organization (WHO). WHO statement on caesarean section rates. 2015. Available from: https://apps.who.int/iris/bitstream/handle/10665/161442/WHO_RHR_15.02_eng.pdf?sequence=1 [Accessed 27th March 2021].

71. National Institute for Health and Care Excellence (NICE). Caesarean Birth: NICE guideline [NG192]. 2021. Available from: https://www.nice.org.uk/guidance/ng192 [Accessed 10th March 2021].

72. Leow HW, Tan EL, Black M. Reported outcomes for planned caesarean section versus planned vaginal delivery: A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2021;256:101-8.

73. Larsson C, Saltvedt S, Wiklund I, Andolf E. Planned Vaginal Delivery Versus Planned Caesarean Section: Short-Term Medical Outcome Analyzed According to Intended Mode of Delivery. *Journal of Obstetrics and Gynaecology Canada*. 2011;33(8):796-802.

74. Geller EJ, Wu JM, Jannelli ML, Nguyen TV, Visco AG. Neonatal outcomes associated with planned vaginal versus planned primary cesarean delivery. *J Perinatol.* 2010;30(4):258-64.

75. Harrison W, Goodman D. Epidemiologic Trends in Neonatal Intensive Care, 2007-2012. *JAMA Pediatr.* 2015;169(9):855-62.

76. Braun D, Braun E, Chiu V, Burgos AE, Gupta M, Volodarskiy M, et al. Trends in Neonatal Intensive Care Unit Utilization in a Large Integrated Health Care System. *JAMA Netw Open*. 2020;3(6).

77. Warren JB, Anderson JM. Newborn respiratory disorders. *Pediatr Rev*. 2010;31(12):487-95.

78. Ziegler KA, Paul DA, Hoffman M, Locke R. Variation in NICU Admission Rates Without Identifiable Cause. *Hosp Pediatr*. 2016;6(5):255-60.

79. Craig JW, Glick C, Phillips R, Hall SL, Smith J, Browne J. Recommendations for involving the family in developmental care of the NICU baby. *J Perinatol*. 2015.

80. Wigert H, Johansson R, Berg M, Hellström AL. Mothers' experiences of having their newborn child in a neonatal intensive care unit. *Scand J Caring Sci*. 2006;20(1):35-41.

81. Noergaard B, Ammentorp J, Fenger-Gron J, Kofoed PE, Johannessen H, Thibeau S. Fathers' Needs and Masculinity Dilemmas in a Neonatal Intensive Care Unit in Denmark. *Adv Neonatal Care*. 2017;17(4).

82. Prouhet PM, Gregory MR, Russell CL, Yaeger LH. Fathers' Stress in the Neonatal Intensive Care Unit: A Systematic Review. *Adv Neonatal Care*. 2018;18(2):105-20.

83. Zenzmaier C, Leitner H, Brezinka C, Oberaigner W, Konig-Bachmann M. Maternal and neonatal outcomes after induction of labor: a population-based study. *Arch Gynecol Obstet*. 2017;295(5):1175-8.

84. Baud D, Rouiller S, Hohlfeld P, Tolsa JF, Vial Y. Adverse obstetrical and neonatal outcomes in elective and medically indicated inductions of labour at term. *J Matern Fetal Neonatal Med*. 2013;26(16).

85. Teitler JO, Plaza R, Hegyi T, Kruse L, Reichman NE. Elective Deliveries and Neonatal Outcomes in Full-Term Pregnancies. *Am J Epidemiol.* 2019;188(4):674-83.

86. de Vries BS, Barratt A, McGeechan K, Tooher J, Wong E, Phipps H, et al. Outcomes of induction of labour in nulliparous women at 38 to 39 weeks pregnancy by clinical indication: An observational study. *The Australian & New Zealand journal of obstetrics & gynaecology*. 2019;59(4):484-92.

87. Gerli S, Favilli A, Giordano C, Bini V, Di Renzo GC. Single indications of induction of labor with prostaglandins and risk of cesarean delivery: a retrospective cohort study. *The journal of obstetrics and gynaecology research*. 2013;39(5):926-31.

88. Sigurðardóttir R, Jónsdóttir RB, Thorlacius MÓ. Upphaf þjónustu við veika nýbura á Íslandi - stofnun Vökudeildar. *Tímarit hjúkrunarfræðinga*. 2019;2(95):70-4.

89. Snædal G BG, Sigvaldason H. Obstetrics and Perinatal Medicin in Iceland 1881-1971 with a Detailed Report on Deliveries in Iceland 1972-1974. Acta obstetricia et gynecologica Scandinavica. 1975.

90. Landspítali. Vökudeild: Nýbura og ungbarnagjörgæsla. 2021. Available from: https://www.landspitali.is/sjuklingar-adstandendur/deildir-og-thjonusta/vokudeild-nybura-og-ungbarnagjorgaesla/ [Accessed 10th March 2021].

91. Sjúkrahúsið á Akureryri. Sjúkrahúsið á Akureyri: Ársskýrsla 2018. 2019. Available from: https://www.sak.is/is/um-fsa/rit-og-skyrslur/arsskyrslur [Accessed 10th March 2021].

92. Kristjánsdóttir GSKKJMEG. Nýburar í áhættumati á vökudeild: Lýsandi rannsókn á eftirliti eins árgangs. Tímarit hjúkrunarfræðinga. 2011;87(4).

93. Embætti Landlæknis. Fæðingaskrá (Birth Register) Available from: https://www.landlaeknir.is/tolfraedi-og-rannsoknir/gagnasofn/gagnasafn/item12340/Faedingaskra-(Birth-Register) [Accessed 5th December 2020].

94. Danilack VA, Triche EW, Dore DD, Muri JH, Phipps MG, Savitz DA. Comparing expectant management and spontaneous labor approaches in studying the effect of labor induction on cesarean delivery. *Ann Epidemiol.* 2016;26(6):405-11.